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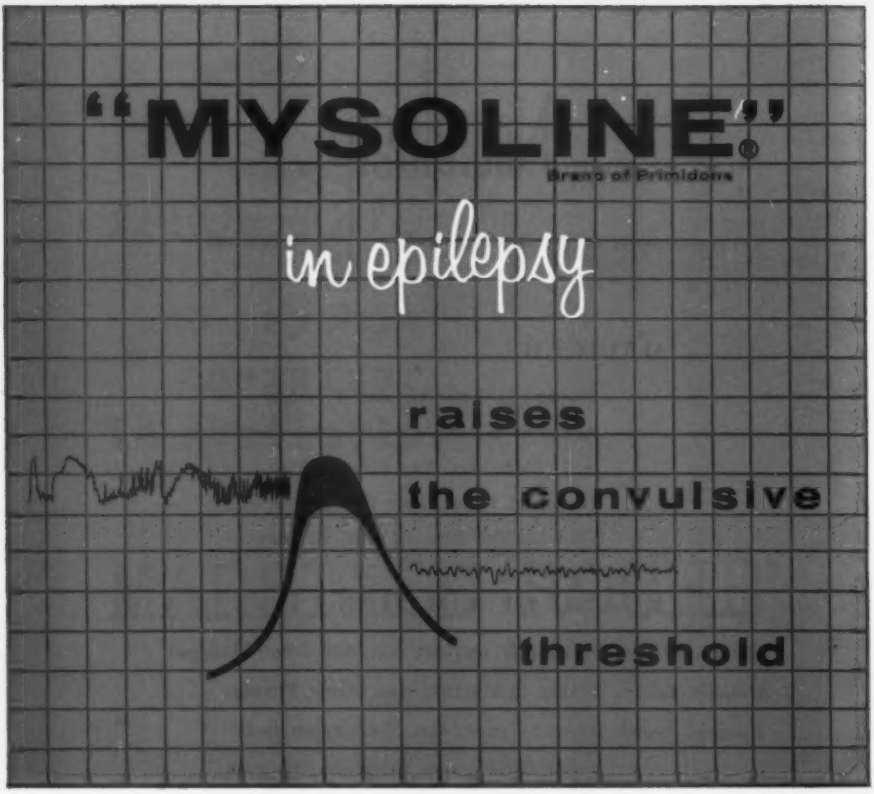

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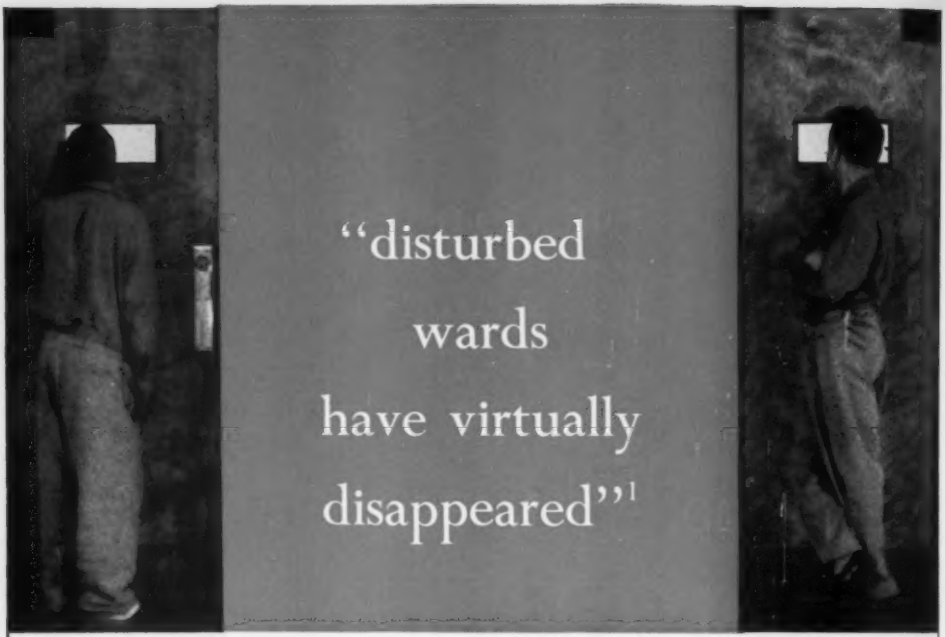

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Neurology Volume 7 • Number 9

Brain Abscesses

A Review of Ninety-Nine Cases

Eugene Loeser, Jr., M.D. and Labe Scheinberg, M.D.***

THE ADVENT and widespread usage of chemotherapeutic and antibiotic agents have produced favorable changes in the clinical picture and prognosis of most infectious diseases. Since brain abscess is frequently secondary to infections outside the central nervous system, it is reasonable that improvement in therapy of primary infections should be reflected in the outcome of central nervous system suppuration.

The purpose of this study is to review the change in mortality of brain abscess coincident with the period of advances in the field of antibacterial therapy. The problem of alteration in the clinical picture of brain abscess by the use of these agents will be investigated and the results compared with those reported during the pre-antibiotic period.

MATERIAL

The records of 99 patients with proved brain abscesses that form the subect of this study were taken consecutively from 1940 through 1956 from the autopsy and surgical files of the Columbia-Presbyterian Medical Center. In order to evaluate results, these cases are divided into three periods: the first, from 1940 to 1944, comprising 49 patients, corresponds to the "sulfa period;" the second period, from 1945 to 1949, with 22 cases, corresponds to the "penicillin period;" the third period, from 1950 to 1956, with 28 cases, represents the era of widespread use of broad-spectrum antibiotics.

The age range in this series of brain abscess was from nine days to 68 years, with the majority distributed in the first four decades (figure 1). This is comparable to the age distribution seen by Evans[1] in a series of 194 brain abscesses between 1908 and 1926. In his series the highest incidence also occurred in the first four decades of life, with a peak in the second decade. It is of interest that only six cases (3 per cent) in his series were seen after age 50, while in the present series 20 per cent of the patients were past 50. Atkinson,[2] in reviewing 23 cases, and Webster and Gurdjian,[3] reviewing 20 cases, noted age distribution similar to the present series.

The sex distribution was 64 males and 35 females. The distribution previously reported varied from a slight male preponderance to a four to one ratio, with generally about twice as many males as females involved.[3–5] The increased risk of trauma in males explains only a small proportion of this preponderance.

SITE OF PRIMARY INFECTION

Other authors,[3,5–13] in considering the relationship of brain abscess to the site of primary infection, have noted a high incidence of mastoid and sinus infections and a relatively small percentage of cases in which the primary site was unknown. Although Macewen[14] gave no definite figures on the site of the primary infection, about two-thirds of his cases were related to mastoiditis. Atkinson[2] implicated the mastoid in 80 per cent of his cases. The sites of primary infection in other series, as compared to the present, are shown in table 1.

The notable differences in the present study are 1) the high incidence of cases in which the primary site was uncertain and with indi-

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TABLE 1

PRIMARY SITES OF INFECTION IN BRAIN ABSCESS, COLLECTED FROM THE LITERATURE AND IN THE PRESENT SERIES

Author	Total	Ear	Sinus	Lung	Metastatic(a)	Trauma	Face Etc.(b)	Post-operative	Unknown	Other (c)
PRE-ANTIBIOTIC										
Evans[1]	194	57%	6%	11%	12%	4%			9%	1%
Atkinson[2]	23	80%								
Sanford[23]	19	26%			21%	21%(d)				
Woltman[13]	18	50%	6%	11%	17%		11%		6%	
Bucy[6]	17	41%		17%	12%	12%	18%			
Courville[20]	76	46%	7%	16%	11%		7%	3%	13%	
Ballantine[5]	31	19%	23%	32%	3%	6%				
PRE- AND POST-ANTIBIOTIC										
Davidoff[10]	34	56%	32%		12%					
Alpers et al.[19]	19	26%	16%	36%	10%				10%	
Pennybacker[4]	110	42%	9%	19%	14%	9%	7%			
Erasmus[12]	29	24%	17%	10%	10%	20%	7%		2%	3%(e)
Botterell[11]	27	44%	30%		11%	7%		7%		
Webster et al.[3]	20	30%	30%	15%		20%			5%	
POST-ANTIBIOTIC										
Ballantine[5]	29	45%	10%		24%	7%		3%	10%	
Present series	99	13%	13%	12%	11%		7%		26%	17%(f)

(a) Metastatic includes distant sites other than lung and includes endocarditis.
(b) This includes face, scalp, etc., infections and may include some cases which were posttraumatic osteomyelitis, but this was not definitely stated.
(c) This includes some unusual or indefinitely stated sites or multiple sites.
(d) This includes birth trauma in this series.
(e) An abscess said to be postmeningitis.
(f) In the present series this includes cases wherein there was more than one site possible as the primary, e.g., patient with empyema and mastoiditis.

cations of more than one infection that could be implicated as the primary one (17 per cent); 2) the high incidence of abscess with no demonstrable site of primary infection (26 per cent); and, 3) a low incidence of mastoid infection (13 per cent).

A history of preceding otitis, mastoiditis, sinusitis, bronchiectasis, empyema, scalp infection, endocarditis, osteomyelitis, and so on, or definite evidence on physical examination, roentgenologic examination, or autopsy of active infections at these sites, were considered criteria for the acceptance of a primary site of infection.

Webster and Gurdjian[3] stated "cerebral abscesses with unknown etiology are rare. Deficiency of either the clinical or pathological examination has been held as accounting for failure to associate cause with effect." Of the 26 cases in the present series in which no primary infection could be documented, 13 presented as intracranial mass lesions, with no suggestion of past or present infection to aid in the preoperative differential diagnosis. This group suggests that, in the present era of widespread usage of antibiotics, a certain number of extracranial infections are treated and may be overlooked at a later date or leave no evidence of their pre-existence at the time the patient is seen with symptoms referable to the brain abscess.

As previous studies have shown, paranasal sinus infection tends to lead to suppuration in the anterior regions of the brain, while mastoid infections spread to the temporal lobe and midportion of the cerebrum, as well as to the cerebellum[6, 10–12, 15] (table 2). The cerebral hemispheres are predominantly involved when those abscesses secondary to mastoiditis are considered alone. Atkinson[2] stated that the ratio of cerebral to cerebellar involvement was about two to one, and in other large series[3, 7, 9–11, 14, 15]

TABLE 2

SITE OF BRAIN ABSCESS IN RELATION TO SITE OF PRIMARY INFECTION

Site of Primary Infection	Anterior	Middle	Posterior	Cerebellum	Thalamus Basal Ganglia	Multiple	Diffuse	Total
Sinus	10	1	1			1		13
Mastoid		8		2		2	1	13
Scalp	3	4						7
Lung	5	4				2	1	12
Metastatic	5	2	2		1	1		11
Other	6	6	2	2		1		17
Unknown	9	9	4		1	2		25
Total	38	34	9	4	2	9	2	98*

*1—from unknown site recorded as being in "lateral ventricle."

the cerebral hemispheres were involved in 76 to 89 per cent of cases. Seven cases were reported by Erasmus,[12] however, in which all the otogenic abscesses were located in the cerebellum.

Brain abscesses of metastatic origin are most often located in the cerebral hemispheres[3,4,7,12,15] in the distribution of the middle cerebral artery, though occasionally in the cerebellum. Other parts of the brain are infrequently the site of abscess, although the basal ganglia, thalamus, and brainstem have been involved in a few cases.[6,10,14] In the present series two brain abscesses were located in the thalamus and basal ganglia, one of which was metastatic and one from an unknown primary infection. No example of brainstem abscess occurred in this study. There were nine discrete multiple brain abscesses. Pennybacker and co-workers[7] reported four multiple abscesses in 31 cases of metastatic origin, while Collis[4] cited the literature stating that 39 per cent of the abscesses secondary to thoracic infection were multiple. In his own series of 44 cases, 48 per cent were multiple.

ORGANISMS

The organisms reported as most frequent have been staphylococcus, streptococcus, and pneumococcus,[3,4,6,7,9,10] although varied organisms have been reported, including actinomyces and Endamoeba hystolytica.[16,17] When a mixed flora has been cultured, gram-positive cocci and gram-negative bacilli have been most frequent. Bucy[9] reported three of 17 cases to be sterile abscesses, and Davidoff[10] reported four sterile abscesses in a series of 32 cases seen from 1930 to 1944. Pennybacker[6] stated that the relative incidence of sterile abscess is commoner today than in former years. Exclusive of sterile abscesses (24 cases), Streptococcus viridans (14 cases) was most frequently encountered in the present series (figure 2).

It is of interest to note that eight of the ten cases of pneumococcus abscesses occurred in the period from 1940 to 1944, while Streptococcus viridans formed a higher proportion of the cultured organisms in the later years.

CLINICAL FEATURES

Incubation Period

The interval between the primary infectious process and the first neurologic manifestation was evaluated in 60 of the 99 cases in this series. In slightly over half of the cases (32) the interval was less than two months; in ten cases the interval varied from two months to one year; and in 18 cases the interval ranged from one and one-half to 20 years.

The interval between primary infection and onset of neurologic symptoms and signs has been evaluated, particularly in cases of brain abscess secondary to lung abscess. Cohen,[18] in discussing such cases, states that lung abscess occurred from four months to four years prior to onset of symptoms of the brain abscess. All but one of his cases had had previous surgery for the lung abscess. Collis,[4] in a review of 44 cases of cerebral abscess secondary to thoracic disease, found no case of brain abscess secondary to an acute lung infection. Ten months was the average interval between diagnosis of empyema and onset of symptoms of brain abscess; eight months was the interval after the diagnosis of lung abscess. Bucy[9] reported a range of one day to six months between the onset of the original infection and the onset of the brain abscess, the majority between one and two months.

Clinical Course

In order to evaluate the duration of the clinical course of brain abscess, the interval between first evidence of cerebral involvement and time of admission to the hospital was determined in 93 cases. Five were in the hospital at the time of first evidence. Of the remaining 88 cases, 29 had a duration of one week or less, 65 one month or less, and 76 two months or less. The longest course was five months. Thus, the clinical course of brain abscesses is distinguishable from the slowly growing gliomas, while simulating the course of a rapidly growing glioblastoma or metastatic tumor.

In Collis'[4] series the course averaged ten to 13 days from first neurologic symptoms to death and in Cohen's[18] series three to 56 days, with more than half having a course of less than ten days from the onset to death. Other authors reviewing brain abscesses secondary to miscellaneous primary infections give statistics similar to those seen in the present series.

Alpers and Foster[19] reviewed the duration of symptoms due to brain abscess in 19 cases, the period ranging from four days to four and one-half months. In all but three cases the duration of neurologic symptoms was 18 days or less. Woltman[13] reported the duration of neurologic symptoms ranging from one week to five months in 18 autopsy-proved cases; in the majority the duration of neurologic symptoms was one to two months. Since these series were from the pre-antibiotic period, it would seem

that the new therapeutic agents have done little to alter the duration of neurologic symptoms, although it is suggested that the interval of time between the primary infection and the onset of neurologic symptoms may now be more variable.

Neurologic Signs and Symptoms

The neurologic symptoms and signs in patients of our series were similar to those seen in other types of intracranial lesions (figure 3). Sixty cases manifested a motor deficit, 56 being hemiparetic or hemiplegic and the four additional having only central facial palsy; 46 patients had papilledema at the time of admission, consistent with the figures of Grant[20] and Woltman,[13] who reported that half of their cases had papilledema when first seen. Twenty-four had aphasic disturbances, 16 a hemisensory deficit, and ten visual field abnormalities. Cerebellar signs were present in two of the four patients with abscess in the cerebellum. One patient developed signs of unilateral parkinsonism as a manifestation of his brain abscess. Convulsive manifestations were recorded in 22 cases.

Physical Signs

In our series there were 28 patients with physical signs of a primary infection, such as discharge from the ear, tenderness over the sinus, and so on (figure 4). In addition, there were 29 who had other positive physical signs, such as cardiac murmurs, cyanosis, clubbing of the fingers, and the like. Forty-two patients had no abnormal signs on physical examination aside from the positive neurologic findings.

Admission temperature was, in general, not helpful in making the diagnosis of an inflammatory mass lesion (figure 5). Only 39 cases had a temperature of over 100° F. rectally; 60 cases were afebrile at the time of admission. Twenty-one had a temperature of over 102° F., of whom over half had signs of meningitis. Other authors have reported the temperature to be usually normal or only slightly elevated.[14,21]

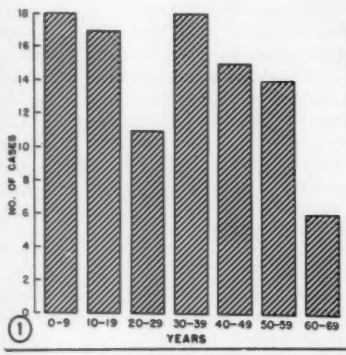
Rapid pulse rate (over 90 per minute) as a manifestation of infection was found in only 36 cases (figure 5). Seven cases had an initial pulse rate of less than 60 per minute as possible evidence of increased intracranial pressure. The pulse rate has been reported as usually slow,[14,21] but this was true in only a small number of cases in our series.

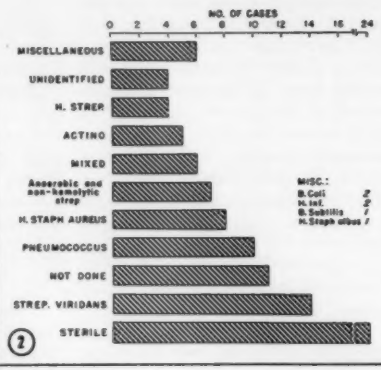
LABORATORY DATA

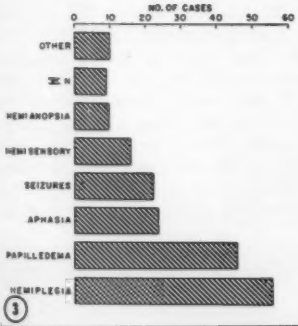
Since the brain abscess was not accompanied by evidence of a primary infection on history or physical examination in many of the cases in this series, the diagnosis was frequently made only at operation or autopsy. Therefore, routine laboratory examinations were reviewed for some clue which might have led to the correct diagnosis (figure 5). Routine tests included complete blood count, spinal fluid examination (unless contraindicated), erythrocyte sedimentation rate, and roentgen examination of the chest and skull.

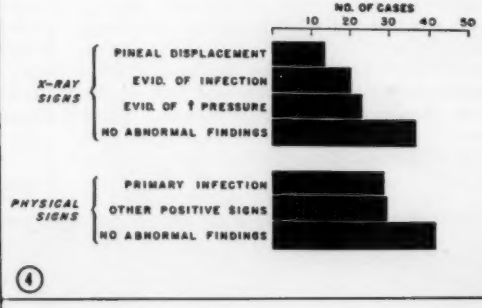
Admission leukocyte count was elevated (over 10,000 per cu. mm.) in 63 of 94 cases in whom results were recorded, being over 20,000 per cu. mm. in 11 cases. The erythrocyte sedimentation rate recorded in 52 cases was elevated in 40 (over 20 mm. per hour Westergren). Thus leukocytosis (two-thirds of the cases) and elevated erythrocyte sedimentation rate (three-fourths of the cases) suggested infection in a significant majority of patients, but there remained a significant group in whom laboratory criteria for the presence of infection was lacking. The erythrocyte sedimentation rate was elevated from 6 to 39 per cent in primary brain tumors and in 55 per cent of metastatic tumors.[22] Hass and Harter,[22] in their analysis of erythrocyte sedimentation rate, found elevation in cases of brain abscess similar to the present report.

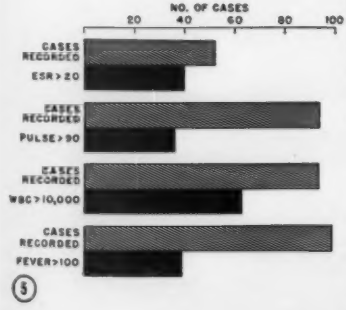
The results of spinal fluid examination are tabulated in figure 6. Lumbar puncture was performed in 72 of the 99 cases. Twenty-one cases (29 per cent) had five or less white blood cells per cu. mm. In seven cases there was a pleocytosis between six and 19 white blood cells per cu. mm., and in 18 cases between 20 and 99 white blood cells per cu. mm. In 14 there were over 1,000 white blood cells per cu. mm. In this group there were three positive cultures and eight spinal fluid sugars under 40 mg. per 100 cc. The spinal fluid protein was recorded in 61 cases and was normal (under 45 mg.) in eight, and mildly elevated (46 mg. to 75 mg.) in 18. Spinal fluid protein was greater than 90 mg. per 100 cc. in 30 cases, of whom 17 also had a pleocytosis over 100 white blood cells per cu. mm. Spinal fluid sugar content was recorded in 41 cases and was reduced in nine cases (less than 40 mg. per 100 cc.). These data are in agreement with the findings of other observers.[6,10,13,21,23,24] Davidoff[10] and Pennybacker[6] found frequent to constant changes in the spinal fluid, particularly an elevation in the protein content. The normal spinal fluid cell count is 29 per cent, and the elevated protein in 80 per cent of the examinations emphasizes the difficulty in the differential diagnosis of brain abscess.











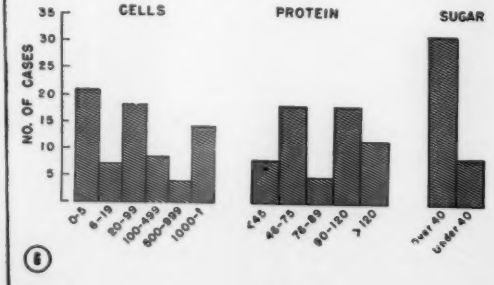


FIG. 1. Age distribution in 99 cases of brain abscess.
FIG. 2. Organisms found on culture of brain abscess.
FIG. 3. Summary of neurologic findings on admission to the hospital in brain abscess.
FIG. 4. Summary of roentgenograms and general physical findings in brain abscess.
FIG. 5. The erythrocyte sedimentation rate, pulse rate, white blood cell count, and temperature recordings on admission to the hospital in brain abscess.
FIG. 6. The cerebrospinal fluid findings in brain abscess. Cell count is white blood cells per cu. mm.; protein and sugar are in mg. per 100 cc.

The results of roentgen examination are tabulated in figure 4. Examination of the skull performed in 73 cases was reported as normal in 37 instances, or slightly more than one-half. Of the remaining cases, 13 showed a significant displacement of the pineal gland and 23 had either local erosion or other evidence of increased intracranial pressure, such as demineralization about the sella turcica or suture separation. Roentgen examination of the chest, the paranasal sinuses, or mastoids revealed evidence of infection in 20 cases. In one case, the finding of a gas bubble at the site of abscess in the temporal lobe was noted (figure 7). Pennybacker[9] also observed this.

Definitive roentgen diagnostic procedures (cerebral angiogram or air study) were performed in 54 cases. Ultimate localization was achieved by ventriculography in 40 cases, by pneumoencephalography in three, and by combined studies in one. In ten cases angiography was the definitive localizing procedure. Twenty-two were operated on the basis of clinical localization alone or on the basis of electroencephalographic findings and two on the basis of plain skull roentgenograms. There were 17 cases diagnosed at the time of autopsy.

In this series preoperative electroencephalography was performed in 41 cases (figure 8); only two cases were reported as normal in this group; eight were diffusely abnormal; and two gave false lateralization. Therefore, the electroencephalogram was specific in 29 of the 41 cases. Localization was possible in 17 of the 29 accurate recordings, lateralization in the remaining 12. The usual abnormalities were the presence of high voltage, slow wave activity. Electroencephalographic findings in 28 of the verified brain abscesses included as part of this series were reported by Ziegler and Hoefer.[25]

RESULTS

The over-all mortality in this series of 99 verified brain abscesses was 47 per cent. Seventeen patients died without surgical intervention and four succumbed following an operative procedure that failed to locate the abscess. There were 30 fatalities among 82 operated cases, an operative mortality of 37 per cent; excluding the four cases in whom operation failed to locate an abscess, the operative mortality was 33 per cent. During period one (1940-1944) when sulfa drug was the primary chemotherapeutic agent, the operative mortality in 36 cases was 47 per cent. In period two (1945-1949) when penicillin was the primary therapeutic agent, the operative mortality

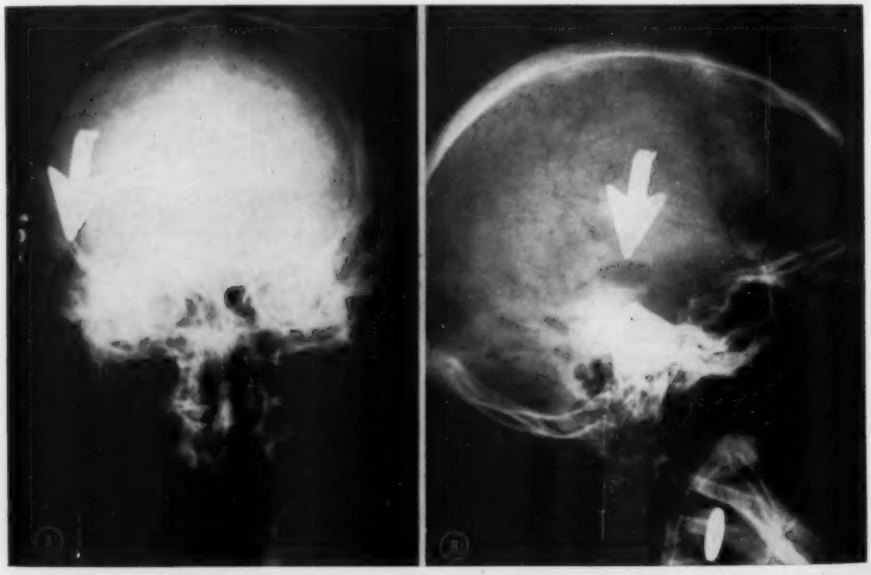
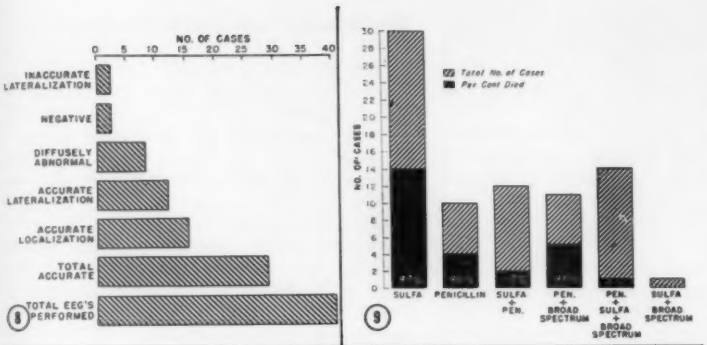


FIG.. 7 Roentgenograms of the skull showing a collection of air lateral to the right temporal horn (arrow). Anteroposterior and lateral views.



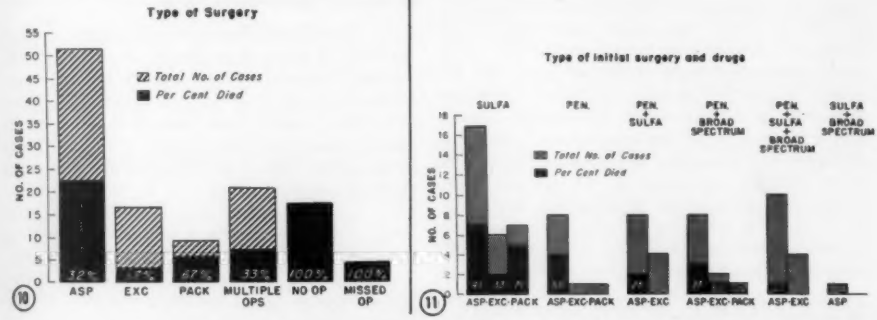


FIG. 8. The results of electroencephalograms in brain abscess.
FIG. 9. The results of surgical therapy of brain abscess correlated with the antibacterial agent or agents used.
FIG. 10. Results of surgical treatment of brain abscess: aspiration, excision, and packing. The results in cases requiring multiple operations are summarized separately. The cases in which no surgical procedure was attempted and those in which the surgical procedure failed to locate the abscess are also shown.
FIG. 11. The results of drug therapy in operated cases of brain abscess.

in 31 cases was 24 per cent; in the latest period 21 cases were operated, with a reduction of mortality to 19 per cent. In addition to the improvement in results in the later years, it was also noted that 11 of the 17 unoperated cases occurred in the 1940-1944 period. In evaluating the operative mortality in this series, all cases were used including those moribund at the time of operation and those in whom the location of the abscess or abscesses would make them ordinarily inoperable.

Results of surgical therapy in brain abscesses without chemotherapeutic or antibiotic agents have been well summarized in a comprehensive review by Webster and Gurdjian.[3] They collected a total of 1,249 patients from 1893 to 1940, of whom 762 died, an operative mortality of 61 per cent. The operative mortality varied from 20 to 25 per cent in a series of four or five cases and 7 per cent in 14 operative cases reported by MacEwen[14] to 100 per cent operative mortality.[17] Pennybacker,[6] in a series of 48 cases prior to penicillin, reported an operative mortality of 46 per cent, and in 62 cases after the introduction of penicillin, an operative mortality of 26 per cent. Ballantine[8] reported two comparable groups of patients: in the period 1936-1940 there was a mortality of 80 per cent, whereas from 1946 to 1950 operative mortality decreased to 34.5 per cent. Results in our series are comparable to those cited above and justify the impression that these agents do improve the over-all therapeutic results in brain abscess.

In order to assess the efficacy of chemotherapeutic and antibiotic agents further, the results of treatment were related to the drug or drugs used (figure 9). Of 30 cases that received only sulfa drugs, the operative mortality was 47 per cent (47 per cent from 1940-1944.) Twenty-two cases that received penicillin with or without sulfa drug had an operative mortality of

27 per cent (24 per cent from 1945-1949). In the 26 cases that received one or more of the broad-spectrum antibiotics with or without other agents, the operative mortality was 23 per cent (19 per cent since 1950).

It can be seen (figure 9) that the best results were obtained from a combination of drugs. There was only one fatality in 14 cases treated with a combination of sulfa, penicillin, and one or more of the broad-spectrum antibiotics.

Surgical procedures performed in these cases can be divided into three groups: aspiration, packing, and excision (figure 10). The most common initial procedure was aspiration with or without drainage. In this series 52 cases were so treated, with an operative mortality of 32 per cent. Nine cases were treated by packing (unroofing or fungus method[26]), with an operative mortality of 67 per cent, and 17 were treated by excision, with an operative mortality of 17 per cent. An average operative mortality of 50 per cent was reported by Webster and Gurdjian[3] in reviewing aspiration as a primary procedure in the pre-penicillin years, whereas in the same period unroofing or packing resulted in an operative mortality of only 21 per cent, as compared to the 67 per cent in the present series. There were 23 cases treated by excision in the pre-penicillin years, as reported by Webster and Gurdjian,[3] with an operative mortality of only 19 per cent. There were seven deaths in 21 cases in whom multiple operations were required.

The results from the three types of surgical procedures related to the use of drugs are summarized in figure 11. Aspiration combined with sulfa drug therapy resulted in 41 per cent mortality. The addition of penicillin caused only a reduction to 37 per cent (six deaths in 16 cases), but the addition of broad-spectrum antibiotics resulted in an operative mortality of 22 per cent (four deaths in 19 cases). Although the number of patients treated by excision or aspiration is relatively small, the operative mortality appeared to be improved by the combination of sulfa, penicillin, and broad-spectrum antibiotics.

The location of the cerebral abscess had no effect on the mortality. Approximately one-third of the cases died, regardless of whether the abscess was in the anterior, middle, or posterior position of the hemisphere. A previously reported case[27] associated with a congenital dermal sinus and supratentorial suppuration was the only fatality among the four cases of cerebellar abscess. There were six deaths in eight operated cases with multiple abscesses.

The site of the primary infection in contrast to the site of the abscess had a significant effect on the operative results. The highest operative mortality was seen in cases secondary to lung abscess, 62 per cent mortality in a group of eight cases. Similar results have been reported elsewhere.[4,6,7,28] A 50 per cent operative mortality occurred in abscess secondary to mastoid infection. Ballantine[8] reported 67 per cent mortality without penicillin and 30 per cent mortality in 13 cases with penicillin therapy. Brain abscess secondary to sinus infection in this series resulted in 17 per cent mortality in 12 operated cases.

SUMMARY AND CONCLUSIONS

1. The clinical features and results of treatment of 99 cases of surgically or pathologically verified brain abscesses studied in a 16 year period between 1940-1956 are reviewed. These cases are divided into three five-year periods corresponding to the years in which sulfa drugs, penicillin, or broad-spectrum antibiotics were in common usage.

2. The age of the patients ranged from nine days to 68 years, with a higher frequency in the older age group than previously reported. There were 64 males and 35 females. This preponderance of males has been reported by previous observers and is, as yet, unexplained.

3. An abscess was present in a relatively high number of cases (26 per cent) without evidence of previous infection. It is suggested that the previous infection may have been suppressed by the use of antibiotics and chemotherapeutic agents, leaving no clue to the nature or the source of intracranial disease. There has been no change in the site of brain abscess since the introduction of antibiotics.

4. A high proportion (24 cases) of the abscesses in this series were sterile. Pneumococcus has declined in frequency from abscesses cultured since 1944, with an increase in the frequency of Streptococcus viridans since that time.

5. The clinical course from the time of the primary infection to the first symptom of intracranial involvement ranged from two months to over 20 years. Once neurologic symptoms developed, however, the course of the patient was rapidly downhill.

6. The temperature and pulse rate on admission to the hospital were of little value in indicating the presence of a suppurative process. The white blood count and erythrocyte sedimentation rate, however, were elevated in

two-thirds and three-fourths of the cases, respectively.

7. The spinal fluid cell count was five or less in 21 cases and over 1,000 white blood cells per cu. mm. in 14 cases. The protein was elevated in 48 of 61 examinations. The sugar was less than 40 mg. per 100 cc. in nine cases, eight of which also had over 1,000 white blood cells per cu. mm.

8. Thirty-six of 73 roentgenograms were abnormal; 13 showed pineal "shift," and 23 revealed erosion or increased intracranial pressure. The electroencephalogram revealed localizing or lateralizing features in 29 of 41 examinations.

9. The average surgical mortality in this series was 37 per cent, with successively better operative results in later years. When antibiotic and chemotherapeutic agents are considered, there is improvement in results with advances in the development of antibacterial agents from sulfa drugs to penicillin to broad-spectrum antibiotics. The best results were obtained with a combination of sulfa, penicillin, and broad-spectrum drugs.

10. The most favorable results were obtained when the abscess was excised. Aspiration with or without drainage was, however, most frequently employed. Abscesses secondary to lung suppuration had a 62 per cent mortality, while cases secondary to mastoid infection had a 50 per cent mortality. Cases in which sinus infection was primary had only a 17 per cent mortality.

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Postchordotomy Studies of Pain Threshold

*Robert B. King, M.D.**

SPINOTHALAMIC TRACTOTOMY has become a well established neurosurgical procedure for the relief of intractable pain. However, reports indicate that 10 to 30 per cent of these patients are either not totally or not permanently relieved of pain by this procedure. The failures have shown a number of disturbing clinical findings, including falling and fading levels of analgesia, spotty areas of hypalgesia below the level of analgesia, and recurrent pain related to analgesic areas.

Over the course of the last three years patients have been selected for study with electrical stimulation in an attempt to further define the changes in sensation which follow this procedure. Only those patients who gave consistently reliable reports of threshold values for sensations were studied in detail.

METHODS

In the early phase of this study skin stimulation was used. A monopolar electrode with a 1 mm. silver ball on the end of a coil spring was moved lightly and slowly over predetermined skin areas. In this manner threshold values for touch and for pricking pain were measured. Each threshold value recorded was confirmed by three trials, each falling within one volt of the approximate average. Normal, hypalgesic, and analgesic skin, as judged by the response to repetitive pinprick, were examined. Reproducible results could be obtained at one sitting but varied from day to day, depending presumably on changes in skin resistance. Stimuli were delivered from a Grass stimulator (Model No. 54B) at frequencies of 1 to 100 or more per second. The strength of stimulation was slowly raised to threshold. The duration of each square wave pulse was varied from 0.02 to 2 milliseconds.

Direct nerve stimulation studies were also done. An insulated needle electrode was inserted into the superficial radial nerve of two patients after chordotomy with pinprick analgesia to C_2 and C_5, respectively. An indifferent electrode was strapped to the contralateral arm. Again, stimuli of 0.02 and 2 msec. duration at frequencies of 1, 4, 10, and 40 per second (and in one instance 400 per second) were used, raising the voltage to threshold. A pressure cuff was placed on the arm. After touch thresholds were determined the pressure cuff was inflated to 250 mm. Hg for 35 to 45 minutes, and the thresholds for pricking pain and, finally, burning aching pain were determined during this period of pressure nerve block. Repeat determinations (three for each recorded threshold) were characteristically within a variability range of less than 0.5 volts.

Nitrous oxide in concentrations of 20 to 60 per cent was given to five patients. The threshold studies could be determined with ease and full cooperation under 20 per cent nitrous oxide. Morphine, Demerol, and Pentothal were also given to two of these patients and similar threshold studies were obtained.

OBSERVATIONS

White and Sweet[1] in their recent classical work on pain state that 40 patients, who were tested with bipolar electrical skin stimulation in analgesic areas after a clinically successful chordotomy, all reported unpleasant or painful sensation at voltages of 40 to 140. Threshold values were not compared with those on the normal side, and the other parameters of stimulation were not mentioned.

In general, we have confirmed their observations in our patients. However, in one instance a patient reported a sensation of a "throb" rather than pain when an electric stimulus strong enough to spark to her skin below T_{10} was applied during operation under local anesthesia. Six hours later she reported pricking painful sensation on electrical skin stimulation in the same area at significantly lower values.

Threshold voltage values for pricking pain (figure 1) on the analgesic side were 40 to 50 per cent greater than on the normal side. As a rule, the difference in voltage required to elicit pricking pain at threshold on analgesic compared to normal skin was less than this maximum. In one case followed for 18 months, threshold values for pricking pain on electrical stimulation on the side of analgesia were within the range of variability on the normal side at the 12-month and 18-month examinations.

Twenty per cent nitrous oxide was given to these patients for repeat testing. In five instances where there had been a distinct drop

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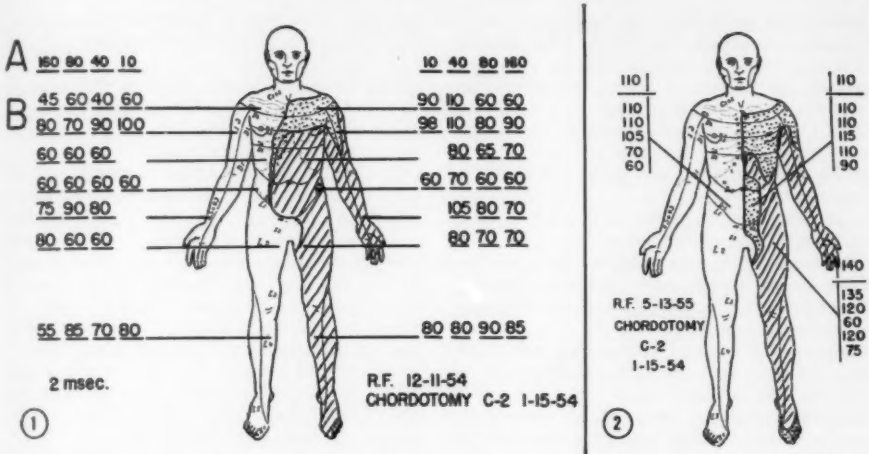

FIG. 1. A 28 year old white male accountant with intractable pain in left flank and leg due to Hodgkin's disease. C_2 chordotomy, right, January 15, 1954. Examination December 11, 1954, patient free of pain. Frequency of stimuli indicated to the right of *A* impulses per second. Voltage for threshold of pricking pain indicated at *B* for the skin areas noted and at each frequency stated at the top of each vertical column of figures. Pulse duration 2 msec. Total pinprick analgesia is indicated in cross hatched area and hypalgesia to pinprick in stippled area. Under 20 per cent nitrous oxide the area of total analgesia to pinprick rose within 12 minutes to the highest level of hypalgesia. The demarcation of pinprick analgesia spreading to the right of the midline between examinations nine months and eleven months later may be due to gliosis at the site of the chordotomy interrupting uncrossed pain fibers. The circle at the left iliac crest indicates an area 1 cm. in diameter in which repetitive pinprick was slightly painful. Other areas of hypalgesia were identified in the perianal region.

FIG. 2. Same patient as figure 1. Examination May 13, 1955. Electrical skin stimulation at 60 per sec. duration 2 msec. Threshold values for pricking pain are indicated in the three vertical columns of figures for skin areas with normal sensation, hypalgesia, and analgesia to repetitive pinprick. The top figure obtained with 100 per cent oxygen and each successive figure with 20 per cent, 30 per cent, 40 per cent, 50 per cent, and 60 per cent nitrous oxide (with oxygen). Contraction of the area of analgesia since the examination on December 11, 1954 (figure 1) is apparent. Pain had returned in the left flank. The perianal hypalgesia on May 13, 1955 extended down the posterior surface of the leg to include the toes. Reliability of reported thresholds was poor with nitrous oxide concentrations greater than 40 per cent. Under 20 per cent nitrous oxide the level of analgesia to repetitive pinprick rose promptly to the highest demonstrated level of hypalgesia. The foot and posterior surface of the leg and buttock were also analgesic to pinprick under 20 per cent nitrous oxide.

in analgesia to pinprick, the level rose quickly to its highest postoperative point. This observation was made in one instance 18 months after unilateral high cervical chordotomy in which the analgesic level had fallen from C_5 to T_8 and, with 20 per cent nitrous oxide, again rose to C_5 within 12 minutes (figure 1). In none of these patients was there a demonstrable change in quality or intensity of pricking sensation in normal skin areas under 20 per cent nitrous oxide, as judged by the patients' descriptions and response to repetitive pinprick. Despite this dramatic rise in the level of pinprick analgesia, there were only minor changes of threshold for "pricking" pain on electrical skin stimulation.

In two instances where the analgesic level fell far enough to allow a return of spontaneous pain, the patients stated that, under 20 per cent nitrous oxide, their spontaneous pain also disappeared with the ascent of the pinprick analgesia.

With increasing concentrations of nitrous oxide the threshold of pricking pain elicited by repetitive electrical skin stimulation of normal and hypalgesic skin areas changed little up to 40 per cent nitrous oxide (60 per cent oxygen) but tended to fall in the analgesic zone (figure 2). When the concentration of nitrous oxide reached 40 per cent or more, the patients might be unable to report consistently reliable threshold values and needed constant prodding to direct their attention to the stimulus.

Further studies are needed using these higher concentrations of nitrous oxide. A normal control, who was trained in repeated test periods and was familiar with detailed reporting of subjective sensations, demonstrated long

latency of perception of repetitive painful stimuli, a build-up of intensity of pain without an increase in voltage once pain was perceived, persistence of pain after stimulation, and fusion of painful stimuli (1 per second) into a constant painful sensation. The threshold for pain was distinctly elevated and remained constant at any given parameter of stimulation.

Burning pain (C fibers) was studied by direct stimulation of the superficial radial nerve after touch fibers were blocked by a pressure cuff. In one patient with clinical analgesia to C_2 (figure 3), threshold values were similar to a normal control subject. On one occasion she complained bitterly of deep aching pain at the top of the pressure cuff (three dermatomes below the level of analgesia) after 31 minutes, and stimulation of C fibers at this time caused severe burning aching pain, sweating, nausea, and great anguish.*

Figure 3 is compiled from two test periods, one with and one without nitrous oxide. The needle placement was sufficiently different on the two occasions so that, when nitrous oxide was given, the threshold for both touch and pricking pain were lower than without nitrous oxide. The ratio, however, between the voltage required to elicit touch and pain was the same. It would appear that during the testing with nitrous oxide the electrode was more directly in contact with the nerve being stimulated under these circumstances. There was marked reduction in C fiber summation under 20 per cent nitrous oxide. Threshold remained almost constant at frequencies of 4, 40, and 400 per second. A control subject, however, showed summation of C fibers of the same degree both with and without 20 per cent nitrous oxide.

To be sure, summation in C fibers occurs between frequencies of 1 and 4 per second and very little summation occurs at frequencies higher than 40. However, the change in slope of the curves for threshold between 4 and 40 per second with nitrous oxide (20 per cent) and without nitrous oxide indicates reduced summation in this frequency range of stimulation.

DISCUSSION

These observations suggest two possible explanations. It may be that an injured or partially sectioned spinothalamic pathway allows passage of well synchronized electrical stimuli and to a lesser degree the relatively unsynchronized impulses generated by repeated pinprick from hypalgesic skin areas. In such a circumstance nitrous oxide may interfere with conduction at the region of trauma enough to block the passage of pinprick stimuli but not those due to brief electrical stimulation.

If these results were due to edema or surgical trauma to unsevered spinothalamic fibers, one would anticipate that the maximum deficit would appear within two or three days and then gradually subside. To be sure, this pattern of recovery may be seen in unsuccessful chordotomies, but these studies carried out weeks to months following the chordotomies suggest that the results are not a reflection of acute surgical trauma. The role of late gliosis as a factor modifying fiber conduction at the site of the lesions cannot be evaluated in the absence of more controlled studies.

An alternative explanation suggests that a pain pathway exists in the spinal cord of man aside from the spinothalamic system. Marchi studies fail to demonstrate a spinothalamic system in cats and dogs, and only a limited number of spinal fibers extending to the thalamus

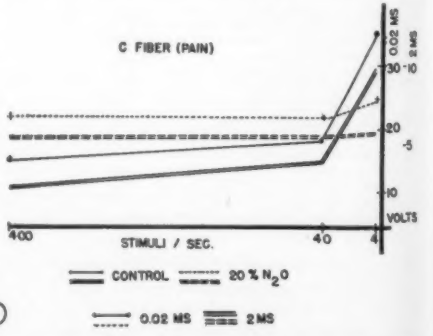

FIG. 3. A 49 year old female, carcinoma of the cervix. Bilateral C_2 chordotomy September 8, 1955. Examination September 18, 1955. Total analgesia to pinprick up to C_2 bilaterally, with hypalgesia over the face which was slightly more pronounced over the first division of each trigeminal nerve than over the second and third divisions. Stimulation of the superficial radial nerve was carried out at 4, 40, and 400 per sec., with pulse duration of 0.02 msec. and 2 msec. slowly increasing the voltage to threshold. Each indicated point on the graph is an average of three or more separate determinations of threshold. This patient was able to identify threshold consistently within 0.5 volt at each determination. Threshold for touch was constant at all frequencies and pricking pain (delta fibers) gave similarly constant threshold values with little evidence of summation. The ratio of voltage (with constant pulse frequency and duration) required to elicit sensations of tingling or throb (touch), pricking pain (delta fibers), and severe deep burning aching pain (C fibers) were similar to those determined in a normal subject using the same stimulating apparatus and electrode.

*White and Sweet[1] described in detail an appreciable incidence of persistent pain from testicular, ovarian, tendon, and periosteal pressure in areas of cutaneous analgesia.

can be shown in monkeys. In cats no constant sensory deficit follows simple section of one anterolateral column of the spinal cord. In these lower mammalian forms there is apparently a multisynaptic system or small unmyelinated fiber system for conduction of pain impulses which is dispersed widely through the cord and may even cross from left to right and back across the spinal cord, as suggested by the observations of Karplus and Kreidl.[2] Gardner and Morin[3] described evoked potentials in the monkey cortex following stimulation of A fibers (larger than 6 to 7 microns) of the lumbodorsal roots so long as either anterolateral quadrant of the cord remains intact.

Nitrous oxide at low concentrations may effectively interrupt such a polysynaptic system without interrupting long fiber pathways. The preferential interruption of long chain systems compared to direct pathways in the central nervous system by drugs has been described in a theoretical presentation by Barany,[4] and has been invoked to explain the depressant effect of drugs on multineuronal paths in the brainstem when primary pathways are unaffected.[5]

Bishop and O'Leary[6] suggested that temporal dispersion occurs in loci of trans-synaptic conduction over complex neuron systems, with consequent interruption of a conducted potential.

Marked analgesic qualities of 20 per cent nitrous oxide have been described and were calibrated as equal to ¼ gr. morphine, using the Hardy, Wolff, and Goodell apparatus to determine pain threshold and pain due to muscle ischemia.[7] Our observations with electrical stimulation show very little change in pain thresholds and an alteration of sensation to pinprick only in hypalgesic areas. In two patients of the group reported here we were not able to determine a reliable change in threshold to electrical stimulation of analgesic skin areas, as contrasted to normal skin areas under morphine (¼ gr.), Demerol (100 mg.), or Pentothal (given intravenously until the patient became drowsy). In these two patients there was no alteration of hypalgesia to pinprick under these drugs. While this experience is too limited to compare the qualities of nitrous oxide with these other drugs, there did not seem to be sufficient evidence that their analgesic qualities could be tested by our present protocol to warrant further effort.

Preliminary studies were commonly carried out prior to chordotomy to establish the patient's evident reliability as a subject for this investigation. This precaution was always practiced if a bilateral chordotomy was to be done. However, if a unilateral chordotomy was contemplated, detailed studies were withheld until the patient was recovering postoperatively and was reasonably comfortable. In such an instance, the normal side was used as a control for the opposite side of the same patient. There was no evidence from these studies that the recent presence of chronic pain and discomfort influenced in any manner the patient's threshold to electrical stimulation so long as undue fatigue and anxiety were avoided. Under these circumstances the patient's ability to identify accurately the same threshold on serial testing diminished and testing was not continued. Kennard[8] has reported similar findings in a detailed study of pain thresholds to electrical skin stimulation in patients with chronic pain, contrasted to pain-free control subjects. The galvanic skin response to painful stimulation was used as a further monitor of pain responses in that study.

Vast differences in "clinical" and "experimental" pain are evident. It is almost impossible to compare a patient's description of clinical pain with his description of pain evoked by electrical stimulation.[9,10] Such an effort is fraught with many pitfalls. Changes of sensation depend on a wide variety of stimulating parameters and technics. The interpretation and accurate description of sensations, for which the subject may find his vocabulary inadequate, depend in part on the patient's anxiety and ability to remain objective in a fluctuating environment or psychologic distractions. For these reasons Wikler[11] and Beecher[12] have encouraged a "multifactorial approach" in studies of pain and its alleviation.

Nonetheless, it seemed necessary in the detailed examination of these patients to bring the study protocol into focus and exclude many technics of investigation while pursuing avenues of promise. Acknowledging the limited approach of the present studies so far as the problem of pain alleviation is concerned, we have used a wide variety of parameters and forms of stimulation and have reported only those observations which have been reliable and reproducible.

SUMMARY

1. Detailed studies of pain thresholds using electrical skin and nerve stimulation indicate that there is a maximum elevation of pain threshold of 40 to 50 per cent for analgesic skin areas following cervical chordotomy.

2. Summation of threshold stimulation of C fibers is absent under 20 per cent nitrous oxide, but is otherwise present after chordotomy.

3. Areas of skin which become hypalgesic to repetitive pinprick after chordotomy again become analgesic to this stimulation under 20 per cent nitrous oxide.

4. A polysynaptic relay pathway for painful stimuli in man, aside from the spinothalamic system, seems probable. The role of late gliosis and an injured though uninterrupted spinothalamic pathway in these subjects cannot be entirely excluded in the absence of pathologic confirmation of these lesions.

The author wishes to acknowledge his indebtedness to Margaret H. Clare, M.A., without whose help and criticism this study would not have been accomplished.

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■ In saying that paralysis without loss of sensation, on the same side of the body, and loss of sensation without paralysis, on the other side of the body, is produced by cutting across a lateral half of the spinal cord, all is not said that has to be said. In such a case there is, in addition, increased temperature and sensibility on the side on which sensation is preserved, and diminished temperature on the side on which sensation is lost, especially if the section be made high up near the medulla oblongata. It would seem, in fact, that the injury has acted on the vaso-motor nerves contained in the cord as well as upon the common motor and sensory nerves, causing paralysis of vaso-motor nerves on the side on which there is increased temperature and anaesthesia. At any rate this mode of explanation is neither impossible nor improbable.

C. B. Radcliffe in *On Diseases of the Spine and of the Nerves*, published in 1871.

Specificity of Facilitatory and Inhibitory Effects of Upper Brainstem Stimulation

George Austin, M.D. and Herbert Jasper, M.D.*

IN THE LAST 15 years the influence of brainstem activity on cortical rhythms and motor function has been a frequent source of investigation. In 1938 Lewey and Gammon[1] showed the excitatory effect of thalamic stimulation on spontaneous activity of resting cortex. Morison and Dempsey,[2,3] in a series of articles commencing in 1942, pointed out that the thalamic reticular system, acting through diffuse thalamocortical projections, is capable of altering cortical electrical activity when stimulated. At lower frequencies of stimuli (6 to 10/s) a generalized synchronization results known as the recruiting response, whereas at higher frequencies of stimulation (greater than 30/s) a desynchronization of cortical rhythm resulted. These results were later confirmed by Jasper and Drooglever-Fortuyn[4] and by Moruzzi and Magoun.[5]

Murphy and Gellhorne[6] in 1945 showed that some hypothalamic regions when stimulated yielded both a facilitatory effect on cortically-induced movement and also a form of facilitation of cortical electrical activity, in that both frequency and amplitude of cortical waves were increased. Rhines and Magoun[7] in 1946 next described regions of brainstem facilitation and inhibition which affected both cortically-induced movement and mechanically-induced reflexes. The effects were present with both flexor reflexes of the foreleg and extensor reflexes of the hindleg. Their descriptions tended to localize these effects to brainstem "areas" rather than to specific nuclei or tracts. Thus, facilitatory regions were generally located anteriorly and inhibitory regions more posterior and medial. Sprague and co-workers[8] showed that, in the decerebrate preparation, facilitation and inhibition from the bulb were exerted on both stretch and flexor reflexes without regard to reciprocal innervation. Altering the frequency of stimulation in no way altered the effective response. In later work, these authors have found evidence for reciprocal effects exerted by lower brainstem stimulation on flexors and extensors.[9] More recently, Hodes, Peacock and Heath,[10] Peacock and Hodes,[11] and Kaada[12] have reported both facilitatory and inhibitory effects from stimulating various subcortical structures.

Several important questions arose from these earlier studies with regard to specificity of stimulation and response. Briefly, the present investigation was undertaken in an effort to clarify and quantitatively answer the following questions which had been raised by previous work: 1) Are there "specific" nuclei and tracts in the upper brainstem which when stimulated cause facilitation or inhibition of movement, or are the effects all of a diffuse nature evoked from stimulation of generalized regions? 2) Do the same sites of facilitation or inhibition of motor and reflex activity have a similar effect on other forms of central nervous system activity, such as respiration and cortical electrical activity? 3) Are these motor effects unrelated to parameters of stimulation, and do they act independently of the sensorimotor cortex? Some of the preliminary results of this work have been described briefly.[13]

METHODS

Experiments were carried out on 52 cats lightly anesthetized with a mixture of Chloralosane, 15 to 20 mg. per kilogram of body weight, and Nembutal, 0.15 cc. per kilogram of body weight. Using a Horsley-Clarke stereotaxic instrument and bipolar steel needle electrodes (75 micra tip diameter, with a separation of 0.75 to 1.0 mm.), the upper brainstem was stimulated and mapped for its effects on cortically-induced movement, cortical electrical activity, and respiration.

Various parameters were used in stimulating the brainstem. Generally, rectangular pulses of duration 0.1 to 1.0 msec. were used and frequency varied from 20 to 500 per second. Stimulating current was noted by measuring the voltage drop through a known resistor, on a cathode ray tube. Occasionally, a 60 cycle sine wave was used. Always the cortically-induced movement was evoked by a 1 second stimulation of 60 cycle sine wave applied to the presigmoid gyrus through silver-silver chloride bipolar electrodes. Intervals of cortical stimuli varied from 10 to 30 seconds and the response was recorded from the opposite hind leg by an isotonic myograph and ink writer.

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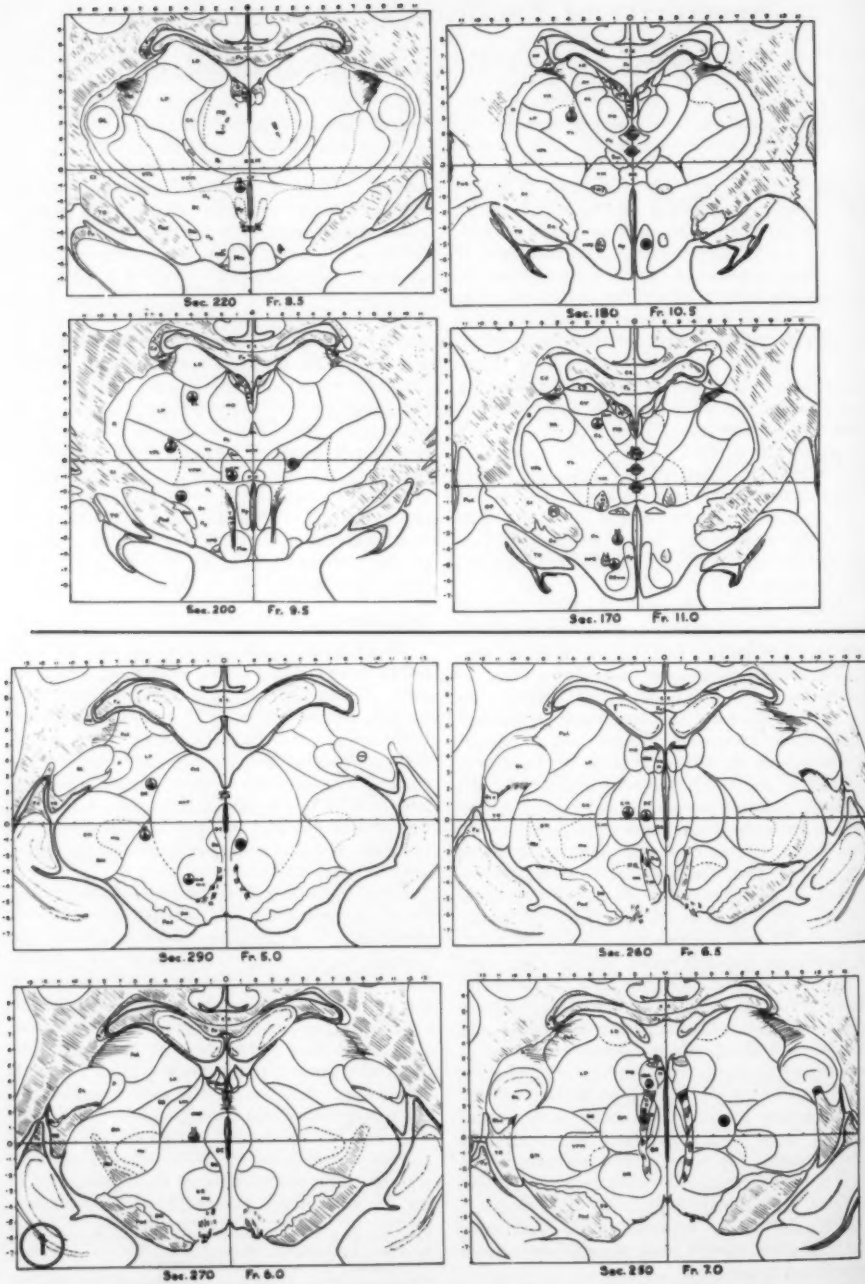


FIG. 1. Horsley-Clarke frontal planes 5.0 to 11.0. On the reader's left are shown facilitatory points and on the right inhibitory points. In the midline are shown points which yielded both facilitation and inhibition (rhomboideus, reuniens, and centralis medialis). "M" indicates that movement was elicited in addition to facilitation or inhibition.

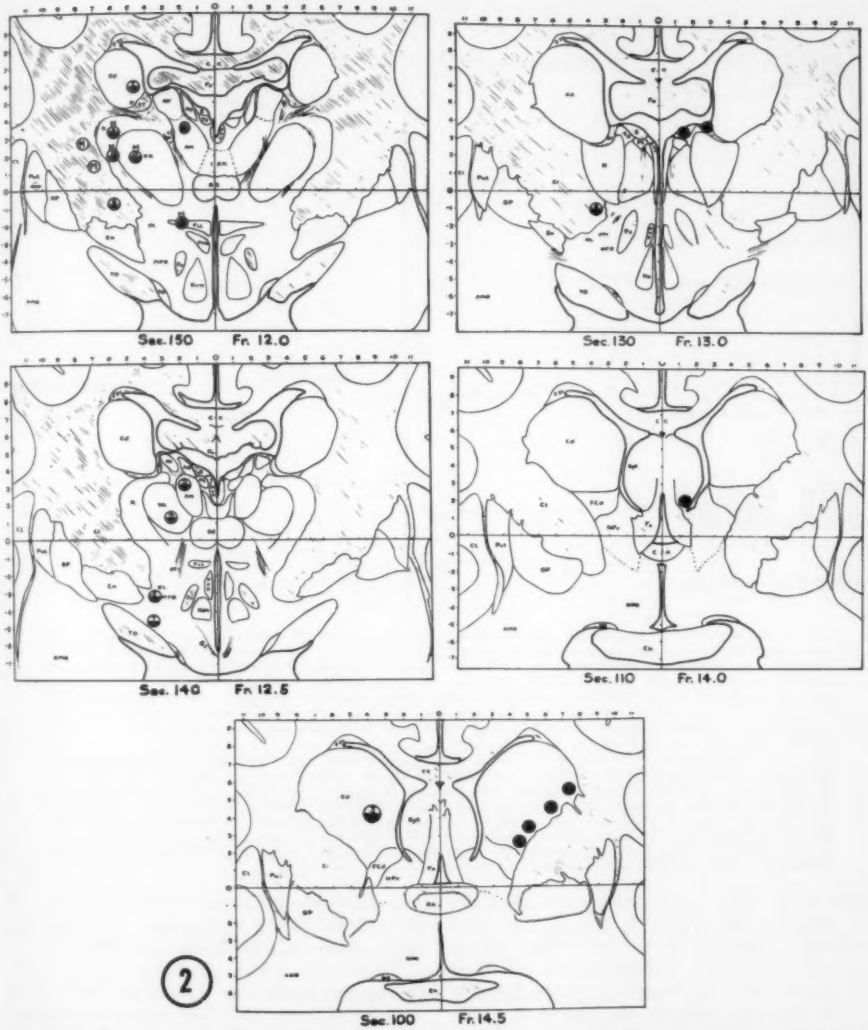


FIG. 2. Horsley-Clarke frontal planes 12.0 to 14.5. On the reader's left are shown facilitatory points, on the right inhibitory points.

Points of stimulation yielding facilitation or inhibition were controlled histologically using the frozen section technic of Marshall.[14] Brainstem stimuli were always kept at a low supraliminal strength to avoid spread of current.

RESULTS

Three different effects were noted on cortically induced movements: 1) facilitation with or without associated movement, 2) inhibition with or without associated movement, and 3) rarely, facilitation or inhibition which reversed to the opposite effect after repeated stimulation.

In figures 1 and 2 are plotted the sites of facilitation or inhibition. They show which nuclei and tracts yielded facilitation on one

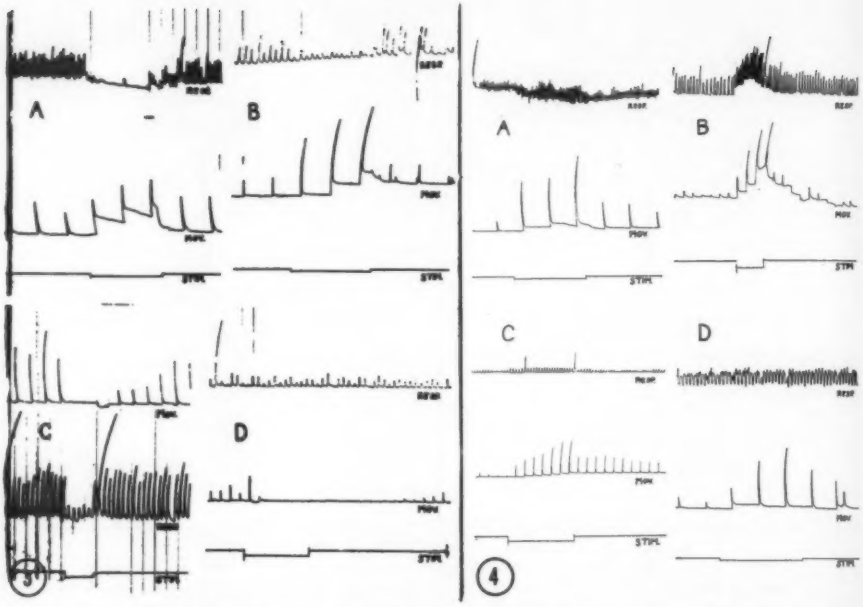


FIG. 3. *A.* Inhibition of respirations with facilitation of cortically-induced movements and increase in tone, from stimulation of nucleus parafascicularis. Cortical stimuli every 30 sec. Stimulus No. 21—Exp. 1-7. *B.* Inhibition of respiratory amplitude with facilitation of cortically-induced movements from stimulation of nucleus ventralis medialis. Cortical stimuli every 30 sec. Stimulus No. 26—Exp. 1-9. *C.* Inhibition of respiratory amplitude with inhibition of cortically-induced movements from stimulation of lateral inferior part of septum. Cortical stimuli every 15 sec. Stimulus No. 34—Exp. 1-4. *D.* No change in respirations with inhibition of cortically-induced movements from stimulation of caudate nucleus (lateral third). Cortical stimuli every 15 sec. Stimulus No. 21—Exp. 1-24.

FIG. 4. *A.* Facilitation of frequency and amplitude of respirations with facilitation of cortically-induced movements from stimulation of internal capsule. Cortical stimuli every 30 sec. Stimulus No. 89—Exp. 1-7. *B.* Facilitation of frequency and amplitude with increase in tone of respiratory movements accompanying facilitation and tonic movement from stimulation of nucleus filiformis. Cortical stimuli every 15 sec. Stimulus No. 81—Exp. 1-19. *C.* Facilitation of amplitude of respirations with facilitation of cortically-induced movements from stimulation of median forebrain bundle. Cortical stimuli every 15 sec. Stimulus No. 30—Exp. 1-16. *D.* No change in respirations with facilitation of cortically-induced movements from stimulations of nucleus reticularis. Cortical stimuli every 30 sec. Stimulus No. 74—Exp. 1-8.

side of the figure and, correspondingly, sites of inhibition on the other side. These cross sectional diagrams of the brainstem extend from Horsley-Clarke frontal plane 5.0 to frontal plane 14.5*. The numbers on the left side of the diagrams indicate the degree of facilitation in hundreds per cent over the amplitude of the test response, considered as 100 per cent. Only those points which yielded complete inhibition of cortically-induced movements have been plotted, hence no number need be given to indicate percent inhibition. Similarly, facilitation less than 100 per cent greater than the amplitude of the test reflex was not plotted. This was decided because we did not consider it significantly increased over the random variation of the test reflex.

Those sites which produced movement in addition to facilitation or inhibition have been marked with an "M." The movement was usually of a tonic type. Several examples of nuclei and tracts producing facilitatory or inhibitory effects are shown in figures 3, 4, 5, and 6. The effects of stimulating the lateral geniculate body and the putamen are included also, although they have not been plotted on the diagrams. The facilitatory and inhibitory effects on dorsal-ventral root reflexes and specific nerve to ventral root reflexes have been described previously.[15] It is sufficient to reiterate that the monosynaptic responses of both flex-

*The brainstem atlas was derived and drawn by H. Jasper and C. Ajmone-Marsan, National Research Council of Canada, 1954

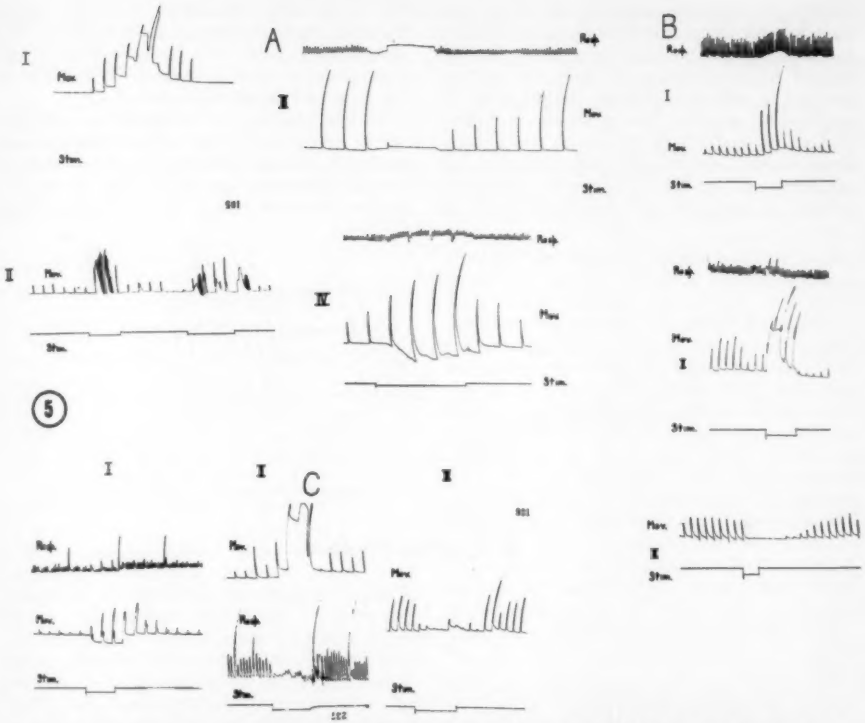


FIG. 5 *A*. I. Facilitation of cortically-induced movement recorded from opposite tibialis anticus, from stimulation of medial posterior commissure. Stimulus No. 4—Exp. 1-2. II. Same as above except recording from the antagonist gastrocnemius. Stimulus No. 9-10—Exp. 1-2. III. Inhibition of cortically-induced movement and also respiration from stimulation of nucleus center median. Stimulus No. 23—Exp. 1-5. IV. Facilitation of cortically-induced movement with no effect on respirations from stimulation of Meynert's tract. Stimulus No. 13—Exp. 1-6. *B*. I. Facilitation of cortically-induced movement from stimulation of putamen. Stimulus No. 118—Exp. 1-19. II. Facilitation of cortically-induced movement from stimulation of nucleus ventralis anterior. III. Inhibition of cortically-induced movement from stimulation of dorsal part of lateral geniculate body. Stimulus No. 130—Exp. 1-19.

FIG. 5. *C*. I Facilitation of cortically-induced movement after bilateral frontal ablation, from stimulation of lateral hypothalamus. Stimulus No. 80—Exp. 1-14. II. Facilitation of cortically-induced movement and inhibition of respirations from stimulation of periaqueductal gray matter. 3.5 volts, 1 msec. pulse duration, 40/sec. frequency. Stimulus No. 6—Exp. 1-40. III. Inhibition of cortically-induced movement from stimulation of nucleus centralis medialis. Stimulus No. 6—Exp. 1-40.

ors and extensors were facilitated or inhibited together.

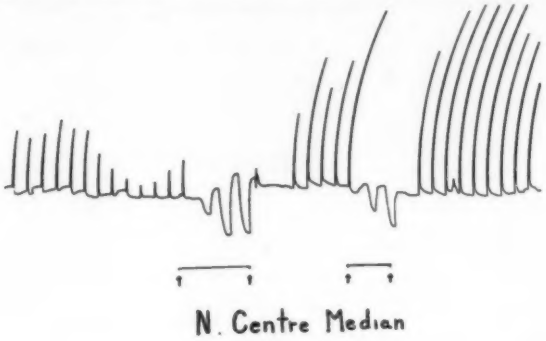
The following effects were noted upon respiration: 1) it was depressed (inhibited) in frequency or amplitude, with either facilitation or inhibition of cortically-induced movements; 2) it was increased (facilitated) in frequency or amplitude with either facilitation or inhibition of cortically-induced movements; 3) it remained unchanged during facilitation or inhibition of cortically-induced movements.

Sites of stimulation which produced respiratory changes have not been plotted on the chart showing the effects on cortically-induced movement. However, the typical forms of respiratory response which have been described are also shown in figures 4, 5, 6, and 7. From the described results it is apparent that the respiratory effects had no direct correlation with the effects produced on cortically-induced movement.

As mentioned in the introduction, many of these different sites of stimulation are capable of altering cortical electrical activity. In this study we were unable to show any direct relationship between facilitatory and inhibitory

activity on cortically-induced movement and the effect on cortical electrical activity. Hence, it was frequently possible, from either facilitatory or inhibitory sites, to drive the cortical rhythms in different portions of the cortex by appropriate stimuli. This is shown in figures 7, 8, 9, 11, and 12. Also, as with respirations, some stimuli which produced facilitation or inhibition of cortically-induced movements evoked no change in the electrical activity of the cortex when stimulated. It would appear then that many of the subcortical sites of stimulation are capable of a multiple function and that control of cortical rhythms is unrelated to the type and degree of motor effect.

To test whether the facilitatory or inhibitory effects on cortically-induced movements were mediated through sensorimotor cortex, bilateral frontal lobectomy was done and movements elicited by stimulating the underlying white



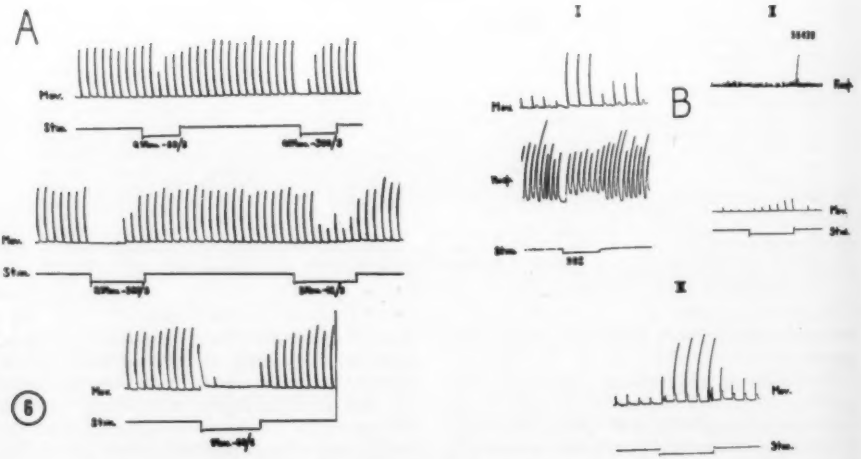


FIG. 6. *A*. Inhibition of cortically-induced movement from stimulation of lateral part of nucl. caudatus, showing the effect of different pulse durations and frequencies of stimulating current. These are all after bilateral frontal lobectomy to show that the pathway of inhibition does not pass through sensorimotor cortex. Stimuli No. 30-34—Exp. 1-23. *B*. I. Facilitation of cortically-induced movement from stimulation of nucl. ventralis lateralis. Stimulus No. 28—Exp. 1-4. II. Facilitation of cortically-induced movement from stimulation of nucl. ant. medialis. Stimulus No. 51—Exp. 1-16. III. Facilitation of cortically-induced movement from stimulation of central tegmental fasciculus. Stimulus No. 5—Exp. 1-1. *C*. Inhibition of cortically-induced movement from stimulation nucl. center median. In addition a slow alternating movement was elicited. Cortical stimuli every 15 sec.

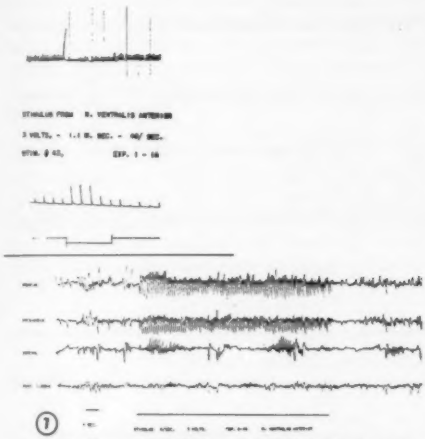


FIG. 7. *Upper.* Facilitation of C.I.M. (evoked every 15 sec.) by conditioning stimulus in nucleus ventralis anterior. *Lower.* Effect on electrocorticogram of stimulation from same electrode position.

matter. The facilitatory and inhibitory sites remained unchanged, although there were occasional variations in the degree. Examples are shown in figures 5C, 6, and 10. The only exceptions were the midline intralaminar nuclei which reversed from inhibition to facilitation after the lobectomy in two instances. The bilateral lobectomy included the anterior and posterior sigmoid gyri and the gyrus proreus.

Facilitatory and inhibitory effects were also distributed bilaterally with equal degree and on both agonist and antagonistic movements. The usual evoked movement from motor cortex was flexion of the foot with contraction of tibialis anticus muscle. As shown in figure 5A, the facilitatory effect was still exerted when the evoked response was changed to extension of the foot with contraction of gastrocnemius.

DISCUSSION

With regard to specificity of stimulus, certain facts are essential in the technic of stimulation. In this investigation the stimulating needles were thinly insulated to the tip. The tip was then bared by rubbing lightly with jeweler's rouge. Thus the area of stimulating electrodes was kept to a minimum. Six needles were arranged in a linear type of electrode, inserted together, and stimulated in pairs. In this way we often obtained a facilitatory or inhibitory response from one pair of electrodes with a decremental response from the pair on either side. Occasionally an opposite response was noted in adjacent pairs, as in the nucleus Ruber, nucleus caudatus, nucleus center median, and nucleus ventralis lateralis, which may be due to the different type cells found in these nuclei. Uniform motor effects were not obtained from any one "system." Although stimulation of the intralaminar group, including center median and reticularis, gives a generalized recruiting response when recording from the cortex, both facilitatory and inhibitory motor effects were found in these regions. Similarly, we cannot say that facilitatory and inhibitory regions of the brainstem tend to be divided into rostral and caudal portions respectively, as others have described.[7,16] Rather, from our studies it appears that there are definite specific regions including nuclei and/or fiber tracts which may cause marked inhibition or facilitation when stimulated under the conditions of this experiment.

Although we have used both nuclear and fiber stains (cresyl violet and Weil), one cannot always be sure whether the effective elements which respond to stimulation are truly nuclei or fibers of passage. However, where we have plotted the response as from nuclei, the site of the stimulating electrode was directly in the nucleus, and we felt as sure as is possible that this was the structure being stimulated.

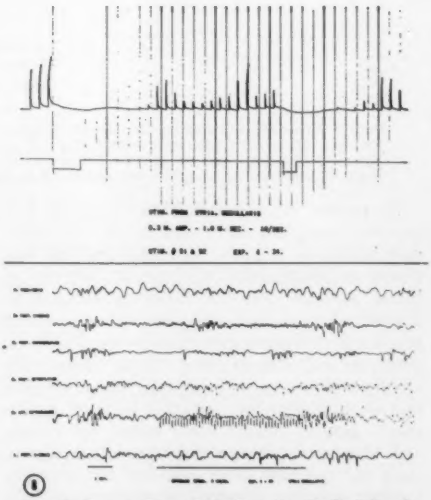
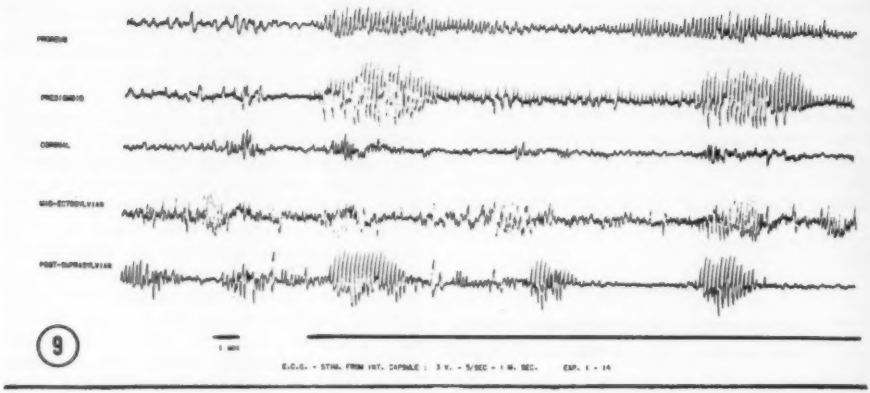


FIG. 8. *Upper.* Shows inhibition of cortically-induced movement from conditioning stimulus in the stria medullaris. Cortical stimuli every 10 sec. *Lower.* Effect on electrocorticogram from stimulation in stria medullaris. The only effect appears to be in the ipsilateral anterior extosylvian area.



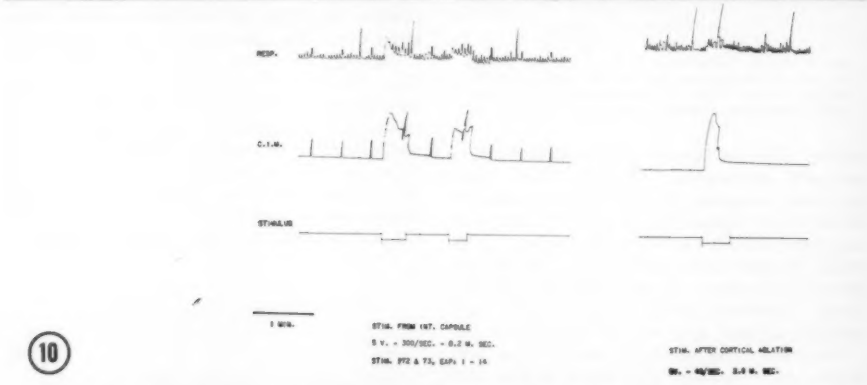


FIG. 9. "Recruitment" response of electrocorticogram from stimulation in the internal capsule.
FIG. 10. Effect on C.I.M. from conditioning stimulus in the internal capsule. Tonic movement is produced but no facilitation from this point. Following sensorimotor cortical ablation, the same degree of movement is produced, showing that the movement is from downstream effects.

In several experiments blood pressure was recorded and, in a fair sampling of facilitatory and inhibitory regions, we could find no evidence to substantiate the theory that rise in blood pressure was the cause of facilitation. Likewise, in a fair sampling of stimulating regions in different experiments we found no evidence that sensorimotor cortex, unilaterally or bilaterally, was an essential link for facilitation or inhibition of cortically-induced movement. Similar results were noted by Rhines and Magoun in the monkey when they stimulated the pyramid after bilateral sensorimotor cortical ablation. Reversal of effect noted also by others[11] was obtained under two conditions. First, it was noted in experiments involving the midline nuclei when, after several stimuli producing one effect, there was twice noted a reversal of effect (once after lobectomy). Secondly, reversal was observed several times after repeated stimulation of a nucleus at one level when the electrodes were pushed several millimeters deeper and then returned, after a period up to one hour, to the original site. Sometimes the original effect might disappear completely and further stimulation be void of any change in cortically-induced movement. Our feeling about the first situation is only presumptive, but we were stimulating the massa intermedia with notably bilateral wide spread connections. Hence, it does not seem unreasonable for such a region to have dual motor effects depending on the balance of excitation from its other wide spread connections. In the second instance, when returning to a previous site of stimulation, the evidence is strongly in favor

of having damaged some of the original descending connections, possibly in a region where two balanced pathways were close together, with the undamaged giving an opposite result on stimulation. One important factor that must be considered is that of anesthesia. Using light Chloralosane and Nembutal and maintaining the animal in adequate balance with intravenous fluids gave us a reasonably stable preparation. Certainly, some of the discrepancies noted in the literature from brainstem stimulation could be explained by use of deep barbiturate anesthesia or from unstable circulatory conditions.

Considering the variations in cell structure of the sites of stimulation and the extensive cortical and subcortical connections of the upper brainstem, it seems unlikely that facilitation or inhibition of movement would be associated with correspondingly similar responses in either respiration or cortical electrical activity. From these results one is not justified in putting forth a behavioral hypothesis concerning stimulation and connections of these regions. It may only be mentioned that there are multiple patterns of seizure and abnormal behavior which are seen with lesions of these subcortical structures. The work of Hess[17] and

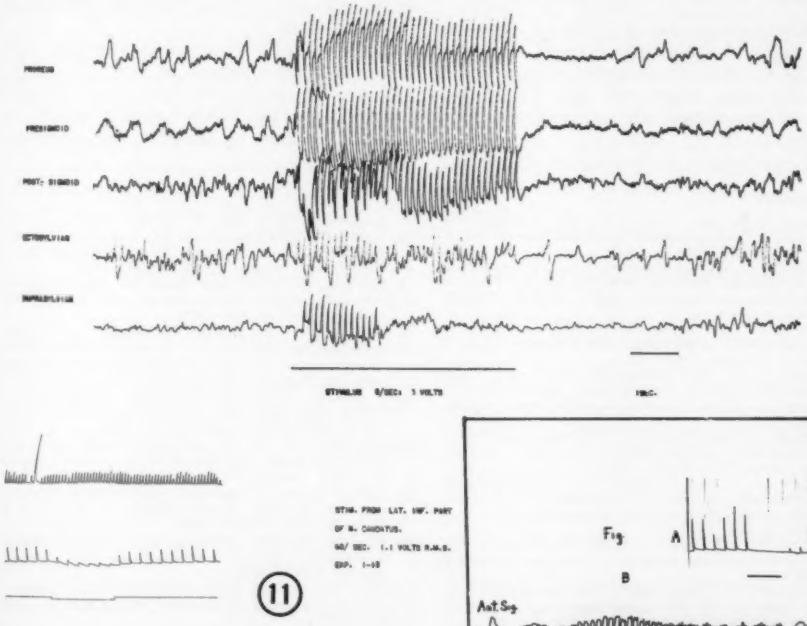


FIG. 11. *Stimulus No. 11. Lower.* Effect of conditioning stimulus in the caudate nucleus on C.I.M., producing inhibition. *Upper.* Effect of stimulus from same electrode site in caudate nucleus on the electrocorticogram.

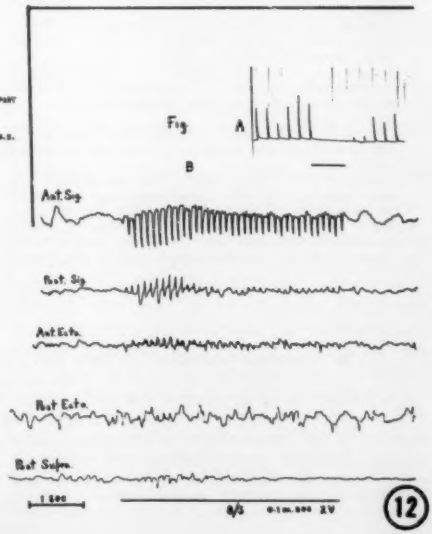


FIG. 12. *A.* Inhibition of C.I.M. from stimulation of medial inferior part of nucleus ventralis lateralis. Cortical stimuli every 15 sec. *B.* Effect on electrocorticogram from stimulation in same electrode position as "A."

Hunter and Jasper[18] stimulating the unanesthetized cat has served to emphasize some of these factors. Phylogenetic development and postnatal conditioning would appear to be other primary factors to be considered in any attempt to understand purposeful organization and activity of the upper brainstem. Finally, the anatomy of internuclear pathways, in addition to ascending and descending pathways, must be further clarified before integrating these findings into a sound hypothesis of behavior under normal and pathologic conditions.

SUMMARY

1. The upper brainstem of the cat has been stimulated and thoroughly mapped quantitatively for its effect on cortically-induced movement; the same region was also studied for effect on respiration and cortical electrical activity.

2. There appear to be sites of stimulation consisting of nuclei or tracts which exert specific facilitatory or inhibitory effects on cortically induced movement.

3. These effects are not necessarily associated with a corresponding facilitation or inhibition of respiratory activity or with equivalent changes in cortical electrical activity.

4. Varying any of the parameters of stimulation has not changed the effect on cortically-induced movement. Also, extirpation of frontal lobes followed by stimulation of the underlying motor fibers did not change the effects of facilitation or inhibition of movement; this implies that the dominant motor effects on cortically-induced movement act downstream on the spinal cord.

5. The evidence obtained suggests that, rather than gross regions of facilitation or inhibition, the upper brainstem seems to show discrete nuclei and tracts having a specific action of facilitation or inhibition on spinal cord elements.

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■ Stertorous breathing has been very generally considered as one of the most dangerous symptoms of apoplexy. Dolaeus observes, that, in the true apoplexy, in which there is an abolition of the animal functions attended with stertor, there is no hope of recovery; yet he afterwards says, that the stertorean and Stentorean respiration is not always fatal; and he relates the case of a person who recovered after having laboured under difficult and stertorous breathing for a whole day. Hippocrates thought that stertor was not always fatal in apoplexy.

John Cooke in *A Treatise on Nervous Diseases*, published in 1824.

A Short Examination for Aphasia

Hildred Schuell, Ph.D.

APHASIC DISTURBANCES constitute an important aspect of clinical neurology and can be expected to increase with the increasing age of the population. Physicians have tended to neglect this area, because examination procedures are complex and results are often confusing. However, there are recurring patterns of aphasic impairment which can be identified by relatively simple testing. These patterns remain consistent if patients are examined after physiologic conditions have stabilized, and each pattern carries a specific prognosis.

Probably 90 per cent of aphasic patients fall into one of five main groups, when classified according to pattern of impairment.[1] *Group I* is characterized by almost total loss of all language functions. In *Group II* only auditory processes are impaired, but this impairment is reflected in defective speech, reading, and writing. *Group III* shows the same pattern as Group II, complicated by specific visual findings. In *Group IV* there is involvement of auditory and sensorimotor processes. *Group V* shows scattered auditory, visual, and motor (usually cranial nerve) findings compatible with generalized brain damage. Some language is usually retained.

Only in Group I, and occasionally in Group V, do patients make errors pointing to common objects named by the examiner.[2] Prognosis for both of these groups is poor; therefore, this test has a high predictive value, although it should not be considered conclusive in itself. Like any other test, it is not reliable if administered while physiologic changes are taking place.

It is the purpose of this paper to present a practical method of examining and classifying aphasic patients, by means of which the physician may determine what cerebral processes are involved, how much recovery may be expected, and what recommendations should be made for treatment.

For most aphasic patients the examination takes 30 or 35 minutes. It is based on tests selected from the research edition of the Minnesota Test for Differential Diagnosis of Aphasia, which is the result of seven years of systematic investigation and exploration of aphasia.[3] Only tests considered to have high diagnostic and prognostic value are included. A short examination cannot be as reliable as comprehensive testing; however, for most patients the selected tests are sufficient for diagnostic purposes.

DESCRIPTION OF TEST

The test has four parts: *Section A*, auditory disturbances; *section B*, visual disturbances; *section C*, speech and language disturbances; *section D*, visual and writing disturbances. No section has more than four tests and, in many cases, these need not all be given.

Section A. Auditory Disturbances. Almost all aphasic patients have some trouble understanding what is said. Some patients have trouble because they do not recognize many words they hear. The first test, therefore, is for auditory recognition. The words used on this test are among the most frequently used words in the English language;[4] therefore, even one or two mistakes signify serious impairment.

Other patients have no trouble recognizing single words, but are able to retain only short sequences of sounds, sometimes only two or three syllables. This is considered impairment of auditory retention span and is explored in test 2. The first two tests are diagnostic. They are prognostic, as well. Patients who confuse the meanings of common words have a poor prognosis. Auditory retention span, however, responds readily to treatment, and as this improves, speech, reading, and writing all tend to improve simultaneously.

Test 3 indicates functional levels of auditory comprehension. It has two parts; the second may be omitted if errors are made on the first.

Section B. Reading Disturbances. Reading disturbances sometimes have a visual component, but are more often on an auditory basis. If a patient cannot recall the word clock when he sees a clock before him, he cannot be expected to recall it when he looks at the printed symbol. However, if he confuses letters and words which look alike and has difficulty following the lines and keeping the place, one may infer that visual processes are impaired.

In Test 1 patients are asked to match printed words to pictures. If a patient can do this, visual recognition is intact. In test 2 patients are asked to point to the word which is spoken

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by the examiner. If a patient makes more errors pointing to words he hears spoken than matching words to pictures, this indicates that the reading disability stems from auditory rather than visual impairment.

Test 3 has two parts and indicates levels of reading comprehension; the second part may be omitted if errors are made on the first. Errors on this test are most commonly related to impairment of auditory retention span. For example, on the sentences: "Do all children like to go to school?" and "Does everyone put money in the bank?," patients who cannot retain the complete series of words often associate children and school and money and bank, and answer yes.

A large source of diagnostic error is the tendency to consider that all reading disabilities indicate involvement of visual processes and to forget that language must be present before reading is possible.

Section C. Speech and Language Disturbances. In this section it is necessary to differentiate between production of speech and recall of language, which is far more complex. Test 1 is an examination for cranial nerve involvement. Unilateral vocal cord paralysis occasionally occurs in conjunction with aphasia. Paralyses of the soft palate, both unilateral and bilateral, and varying degrees of paralysis of the tongue have been found.[1] These diagnoses should not be made unless there is observable deviation or inequality of movements of the two sides, or unless some specific movements (protrusion, retraction, lateral or vertical movements) can never be elicited. These defects are usually accompanied by difficulty swallowing.

If the patient makes errors on test 2, when no paralysis or paresis of the speech musculature is present, this is usually indicative of sensorimotor involvement. Patients with sensorimotor involvement frequently have difficulty initiating, controlling, and coordinating voluntary movements of the speech musculature. They behave as if they did not know where the tongue was in the mouth or how to move it in a desired direction or to a desired position. They are consistently unable to produce sounds which require complex coordinations, and the same sounds tend to be defective whenever they occur. The most valid hypothesis seems to be that this difficulty is associated with reduced kinesthetic and proprioceptive cues.

Inconsistent articulation errors result from imperfect auditory recall, but these do not often appear when patients are asked to repeat short units. For this reason, words on test 2 should be spoken slowly and distinctly and each word is said twice before the patient is asked to respond.

On test 3 patients are asked to name objects. Impairment of naming is a defect of auditory recall. Errors usually consist of words which sound like the given word (approximations or words related to it in meaning (associations). Bizarre and unrelated responses indicate more severe disruption of language processes.

Test 3 requires preservation of only the most frequently used English words.[4] Test 4, for language formulation, demands more extensive vocabulary and use of some of the structural forms of language. This test has two parts; the second may be omitted if errors are made on the first. Errors on this test correlate with impairment of auditory retention span.

The most common diagnostic error in aphasia is the assumption that all impairment of speech stems from motor defects. Speech patterns may be very defective with complete integrity of the motor mechanism, if auditory feed-back is impaired. The disintegration of speech which follows incurrence of severe hearing loss is an example of this.

Section D. Visual and Writing Disturbances. Impairment of visual recall is tested by asking the patient to draw a man and reproduce symbols exposed for two seconds (test 1). Distortions and reversals of symbols indicate severe impairment of visual recall.

Test 2 is a spelling test presented in both written and oral form. If the patient spells words aloud correctly but makes errors writing them, visual recall is impaired. With markedly impaired auditory recall, patients are unable to spell aloud at all and depend wholly upon visual imagery for writing. This results in defective spelling also, but in this case oral spelling is equally or more defective than written.

Test 3 involves writing to dictation. If errors increase as the units increase in length, this indicates impaired auditory retention span.

Test 4 gives the examiner a sample of the patient's spontaneous writing. Aphasic patients tend to write much as they talk, and defective auditory recall and auditory retention span will result in defective written as well as defective oral expression.

The examiner should study all samples of the patient's writing for reversals and distortions of letter forms and substitution of letters which look alike, since mild impairment of

visual recall may not appear on test 1 but will appear on more difficult tasks. These are the only reliable indicators of impaired visual recall, since writing, like reading and speaking, may be exceedingly limited or defective if the auditory patterns of language are impaired.

The examiner need allow for no more than the ordinary amount of awkwardness in the use of the non-preferred hand. Most aphasic patients become extremely proficient writing with the left hand when it is necessary. Difficulties performing movements with the non-paralyzed hand are not usually found with unilateral lesions.

CLASSIFICATION OF PATIENTS

Patients are classified according to the pattern of impairment revealed by test findings and not according to severity of initial involvement. Impairment varies from mild to severe in all groups except Group I. Severity of impairment affects prognosis only to the extent that recovery takes longer when impairment is severe than when it is mild. A description of each of the five clinical groups follows.

Group I: Severe Impairment of All Language Modalities

Diagnostic criteria. There are two essential diagnostic criteria for group I. First, patients make errors pointing to common objects named by the examiner (section A, test 1). Secondly, these patients have no functional speech, reading, or writing. They cannot name objects, answer questions, read, or write, although they can sometimes match simple words to pictures.

Differential diagnosis. Patients in group IV sometimes appear almost as impaired as group I patients on initial testing, except that they do not make mistakes pointing to common objects named by the examiner.

Prognosis. These patients rarely recover functional speech. They can be taught to repeat, copy, and make associative responses. Some reactive speech appears but it does not become voluntary. Auditory comprehension tends to improve with intensive auditory stimulation, but regression takes place when this is discontinued. The poor prognosis for this group is frequently hard to accept, for many group I patients are extremely adequate in situations which do not depend on language. They grasp some words and respond to total situations so well that families usually report they understand everything that is said. They follow directions well if they are shown what to do. They often show social awareness and appropriate social behavior.

Recommendations. A short period of treatment may resolve catastrophic reactions and prevent withdrawal and depression. The same

TABLE 1

Classification	*Findings*	*Prognosis*
GROUP I Severe impairment	1. Impairment of auditory recognition. 2. No functional speech, reading, or writing.	Poor. Can learn to repeat and copy, but language does not become functional.
GROUP II Impairment of reauditorization (auditory retention span, auditory recall)	1. Impairment of auditory retention span. 2. Inconsistent articulation errors resulting from imperfect auditory imagery. 3. Word-finding errors. 4. Reading and writing reflect errors found in speech.	Excellent. Approximate former performance level. Speech, reading, and writing improve simultaneously as a result of auditory stimulation.
GROUP III Impairment of reauditorization with co-existing visual involvement	1. All findings reported for group II. 2. Confusion of letters and words which look alike. 3. Reversals, distortions, and substitutions of letters which look alike found on writing.	Recovery of speech good. Reading and writing slower. Good results not obtained if marked spatial disorientation is present.
GROUP IV Impairment of reauditorization with co-existing sensorimotor involvement	1. Auditory recognition is intact, but impairment of auditory retention span and of auditory recall is frequently severe. 2. Repetition is impaired. Articulation errors are consistent.	Limited recovery. Speech is defective and hesitant and vocabulary frequently limited, but language is functional as acquired. Reading and writing lag behind speech.
GROUP V Scattered auditory, visual, and motor findings compatible with generalized brain damage. Some language functions retained.	1. Patients usually make errors following directions and understanding paragraphs. 2. Reading comprehension reduced. 3. Cranial nerve findings usually present. Slurred speech. 4. Distortions on drawing and writing.	Guarded. Patients often get more speech, but are incapable of sustained effort and do not make consistent progress.

results might be accomplished by the family if they were able to reassure the patient and give him confidence in his ability to function independently within his limitations. Actually, few families are secure enough with the altered condition of the patient to be able to do this, and treatment should be designed to help the family as well as the patient. A long period of treatment is never indicated. Group I patients often receive benefit from self-care, ambulation, and diversional activities. A dependable daily routine and systematic provision for social participation within the patient's limitations are the best safeguards against depression.

Group II: Impairment of Auditory Retention Span and Auditory Recall

Diagnostic Criteria. In group II auditory recognition is intact, but auditory retention span is impaired (section A, test 2). Some speech and some reading and writing are usually preserved but defective. Errors increase in direct relation to the length of the stimulus or the length of response required.

Differential diagnosis. Group II patients may be confused with group IV patients when impairment is severe enough that pronunciation is defective. However, the errors made by group II patients are inconsistent and may be corrected readily by ear. Some speech which sounds normal is usually present or emerges early. Word-finding errors reflect impairment of auditory recall.

Group II patients are sometimes considered disoriented or confused, because word finding and patterns of connected speech are defective. The patient may say Sunday for Monday, January for June, chair for table, or a dime for a dollar. In his effort to find the word he wants, he may produce chains of associations and get far afield. Because auditory retention span is limited, he may forget what he was asked, what he has said, or what he wanted to say. However, within the existing retention span, comprehension is good.

Prognosis. Patients in group II make excellent recovery in all language modalities. Speech, reading, writing, and even arithmetic improve simultaneously as auditory retention span increases. Many are able to return to exacting professions, such as teaching, medicine, or law. Students returning to classes find it necessary to take reduced course loads because reading and writing are slow at first. Many universities have reading clinics which offer effective help.

Recommendations. Group II patients require treatment to obtain maximal recovery. Even when speech sounds normal, patients encounter less obvious difficulties in many areas: listening to radio programs, following lectures, carrying out detailed instructions, remembering names and telephone numbers, performing simple arithmetic computations, grasping material read, or conversing with groups of people. If these difficulties are not anticipated and the patient is not given help in understanding and overcoming his disabilities, he may develop anxieties and fears and withdraw from activities necessary for recovery.

Group III. Impairment of Auditory Retention Span and Auditory Recall with Coexisting Visual Involvement

Diagnostic criteria. These patients have all the symptoms presented by patients in group II, but in addition there is specific impairment of recognition and recall of visual symbols.[5] Drawing a man (section D, test 1) is almost always defective. Reproducing symbols (section D, test 2) frequently shows distortions, reversals, spatial disorientation, and confusion of symbols which look alike, such as *WM, EF, PBR, pbdq, rhnu,* and *ft.* In script, the following groups are commonly confused: *bf, hk, iu, ao, el, wu, gq,* and *jy.* If the visual involvement is mild tests 1 and 2 may be performed normally, but the same signs will appear on more complex writing tasks and should be looked for. There is a tendency toward phonetic spelling, and oral spelling is better than written. With visual involvement, short words are recognized more easily than long words; the opposite tends to be true with auditory impairment, for short words present less distinctive auditory cues. (We scarcely hear words like of, have, is, and was in connected speech.) Group III patients usually do not have trouble matching; visual discrimination is usually remarkably intact when only one discrimination at a time is demanded. Unless the defect is extremely severe there is no difficulty recognizing objects; in recovery, recognition of objects precedes recognition of symbols. Blurring and obfuscation of vision are sometimes reported. All group III patients seen to the present time have had field defects; however, field defects are found in patients who have no impairment of visual recognition or recall.

Differential diagnosis. The important thing is that even severely limited ability to read and write does not necessarily indicate involvement of visual processes. All group III pa-

tients show some of the specific signs described.

Prognosis. The prognosis for recovery of speech is the same as for patients in group II. Reading and writing improve much more slowly. Functional skills are recovered, but little inaccuracies persist and rate of performance is probably permanently retarded for most patients.

Recommendations. Group III patients require intensive treatment, but they are able to work independently with only minimal guidance after speech is re-established. Patients with severe impairment of visual recognition and recall need to relearn individual letter forms. Word recognition is extremely slow initially, because at first the patient is forced to identify each letter and spell the word, but this improves with training. Group III patients should be counselled against trying to return to occupations which place high demands upon speed and accuracy of reading and writing.

Group IV. Impairment of Auditory Retention Span and Auditory Recall, with Coexisting Sensorimotor Involvement

Diagnostic criteria. Diagnosis of sensorimotor involvement is made on the basis of impaired ability to imitate speech patterns (section D, test 2) when there is no paralysis or paresis of the peripheral speech musculature. Short syllables are used and two trials are given to minimize mispronunciations resulting from defective auditory recall.

Differential diagnosis. Many group IV patients have such short auditory retention spans and are so severely impaired in auditory recall that they resemble group I patients, except for the fact that auditory recognition is not impaired.

Group IV patients differ from severely impaired group II patients in that articulation errors are consistent. The same sounds tend to be defective in all words, and sound combinations which require complex coordinations are more defective than sounds with simpler motor patterns. All speech attempts are equally hesitant and labored.

In the beginning group IV patients may have difficulty initiating phonation. Tongue movements may appear incoordinated and the patient may have little voluntary control of the musculature, although no weakness is present.

Prognosis. These patients do not usually make complete recovery. Progress is slow and language remains limited and sometimes defective, but it is functional as it is acquired. Prognosis depends more upon the amount of auditory impairment present than on the severity of the motor involvement itself.

Recommendations. Group IV patients require a long period of retraining. Intensive auditory stimulation is necessary, as well as facilitation of movements.

Group V. Scattered Auditory, Visual, and Motor Findings

Diagnostic criteria. Patients are classified in group V if there is some involvement of auditory processes, some clear-cut visual findings, and some specific sensorimotor or cranial nerve involvement. The latter is more common. The basis of this classification is involvement of all three processes underlying language.

Superficially these patients differ from each other more than patients in any other group, because in some patients one process will be severely involved and in some another is affected. Some may understand fairly well and show only a little slurring of speech, but have severe visual involvement. In others the cranial nerve involvement may be so severe as to almost preclude speech, but visual and auditory processes show only mild impairment.

In age and etiology, these patients showed more similarity than any other group studied. In one sample all group V patients were over 50 years of age, and 75 per cent of the group were over 60. For eight per cent the etiology was severe trauma, for eight per cent arteriosclerosis, and 83 per cent were known hypertensives who had incurred more than one known cerebral episode.[3]

Prognosis. Results which can be obtained from treatment are limited by the physiologic condition of the patient and the amount of generalized brain damage which has been sustained. Most patients showed emotional lability, and few were capable of sustained or systematic effort. Most of them were more concerned about physical symptoms, such as dizziness, headaches, or dyspnea, than about speech. Some of the traumatic cases showed regressive behavior or evidence of organic psychosis. Although few group V patients could work independently, many did very well when working with the clinician, and limited goals, such as increasing intelligibility or vocabulary, could be achieved. This contributed to the adjustment and well-being of the patient.

Recommendations. Whether or not treatment is recommended should be determined

TABLE 2

	Group I *Severe Damage*	Group II *Auditory Retention Span and Recall*	Group III *Specific Visual Findings*	Group IV *Specific Sensorimotor Findings*	Group V *Auditory Visual and Motor Findings*	*Number of Errors*
Section A						
Auditory disturbances						
1. Auditory recognition	Def.	Intact	Intact	Intact		
2. Auditory retention span	Def.	Def.	Def.	Def.	Def.	
3. Auditory comprehension	Def.			Def.	Def.	
a. Directions						
b. Paragraph						
Section B						
Reading disturbances						
1. Word recognition (vis.)			Sig.			
2. Word recognition (aud.)	Def.			Sig.		
3. Reading comprehension		Def.	Def.	Def.	Def.	
a. Sentences	Def.					
b. Paragraphs	No P.					
Section C						
Speech and language disturbances						
1. Cranial nerve		Intact	Intact	Intact	Def. on	
2. Sensorimotor	Def.	Intact	Intact	Def.	1 or 2	
3. Naming	No P.	Sig.	Sig.	Sig.		
4. Functional speech	No P.	Def.	Def.	Def.	Def.	
a. Definitions						
b. Proverbs						
Section D						
Visual and writing disturbances						
1. Revisualization		Intact	Sig.	Intact	Def.	
a. Man						
b. Symbols						
2. Spelling	No P.	Sig.				
a. Written	No P.		Sig.	Sig.		
b. Oral				Def.		
3. Functional writing	No P.	Def.	Def.	Def.	Def.	
a. Dictation						
b. Spontaneous						
c. Reversals, distortions, confusions of symbols		Intact	Def.	Intact	Def.	

Def.: Defective No P: No performance Sig.: Errors significant if present
Blank spaces indicate performance not significant for classification.

by the physiologic and mental condition of the patient. If he shows frustration at his inability to communicate or make himself understood and is reasonably stable physiologically, treatment can be beneficial. Long-term treatment is seldom advisable.

The classifications described above are summarized in table 1. Table 2 presents characteristic test patterns for each group. In this table the designation "errors significant if present" is used for items which are diagnostic, but which may be passed by patients with only mild impairment. It is necessary to include such items, for patients with severe impairment will not be able to perform at all on more difficult tasks.

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DIRECTIONS FOR ADMINISTERING AND SCORING TEST

Before administering the test, the examiner should familiarize himself with the testing procedures and have materials conveniently arranged for presentation. The patient should be relaxed and comfortable. Encouragement should be given freely throughout the examination.

Each item on each test is checked right or wrong as it is administered. It is desirable to keep a record of the number of errors made on each test for purposes of test-retest comparison, since it is often important to know if regression or recovery is taking place. All scoring should be done as the test is administered. This can be done unobtrusively if the patient is placed at the examiner's left.

If the number of errors made on each test is transferred to the right hand column of table 2, an over-all picture of the patient's performance may be obtained and compared with test patterns summarized in this table. When the classification is determined, it should be checked with findings reported in table 1 for verification and prognosis.

When the test has been administered a few times, the examiner will find he has usually arrived at a diagnosis before testing procedures are finished.

EXAMINATION PROCEDURES

SECTION A

AUDITORY DISTURBANCES

1. *Auditory Recognition* *Number of Errors:*

Materials: pencil, match, penny, Card 1, and Card 2.

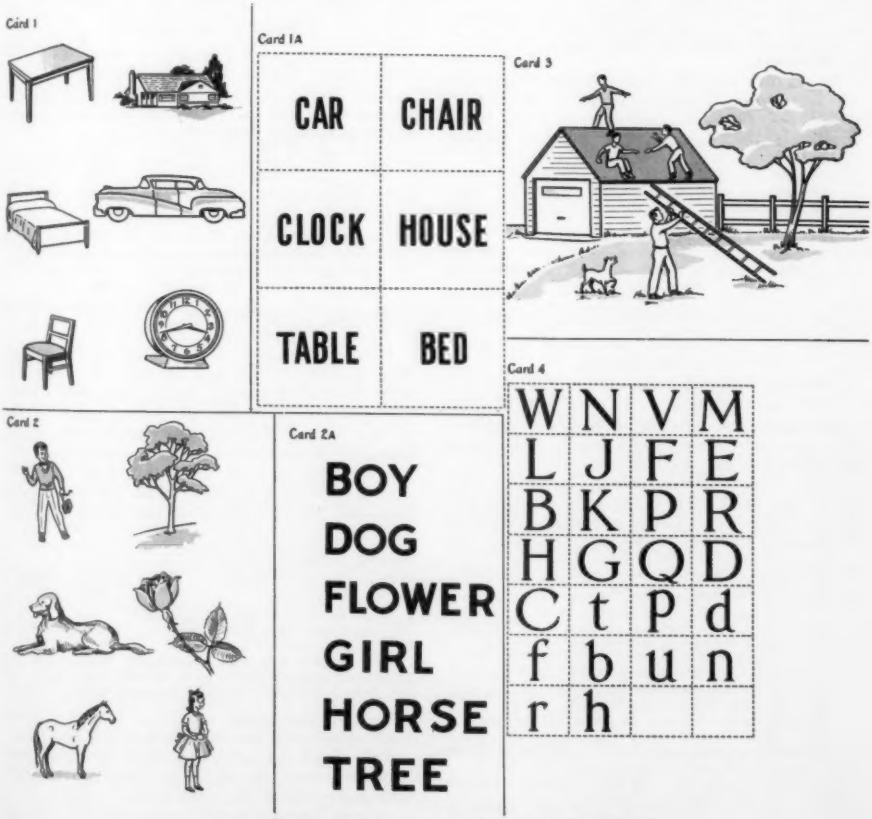

FIG. 1. Test materials to accompany examination for aphasia.

Place the pencil, match, and penny in front of patient. Explain and demonstrate that he is to point to the object you name. In testing, speak only the given word. Say it distinctly, pause, repeat, then wait for patient to respond. When patient understands the procedure, present Card 1. Say: *Car — car;* name objects in order given below. Repeat procedure with Card 2.

(1) car	(4) chair	(7) dog	(10) flower
(2) clock	(5) house	(8) girl	(11) horse
(3) table	(6) bed	(9) tree	(12) boy

2. *Auditory Retention Span*

Use (a) if patient cannot repeat. Use (b) if patient can repeat.

a. *Pointing to objects named serially* *Number of Errors:*

Present Card 3. Say: *Show me the man and the dog.* Repeat: *Show me* before each item. Repeat instruction if patient requests it or seems disturbed because he cannot remember, but score as an error.

(1) the man and the dog
(2) the fence and the ladder
(3) the roof and the door
(4) the door, the man, and the garage
(5) the ladder, the fence, and the tree
(6) the door, the roof, and the grass

b. *Repetition* *Number of Errors:*

Say: *Listen carefully and say just what I say. Are you ready?* Underline words mispronounced, draw a circle around words left out, write in any words which are added. Repeat if patient requests it, but score as an error.

(1) snowman
(2) gingerbread
(3) impossibility
(4) Please sit down.
(5) Will you answer the telephone?
(6) The bus runs every 20 minutes.
(7) He lives in the third house from the corner.
(8) They serve fried chicken, baked ham, and roast beef.
(9) I ordered a ham sandwich, a glass of milk, and a piece of apple pie.
(10) The office is on the twenty-fourth floor of the Merchant's Bank Building.

3. *Auditory Comprehension*

a. *Following directions* *Number of Errors:*

Materials: the following objects are required: bell, cup, open padlock with key in lock, a long and a short pencil, and a spoon.

Place objects before patient in order given above; put them back in the same position after each direction. Say: *Listen carefully and do what I ask you to do.* Repeat direction if necessary, but score as an error.

(1) Ring the bell.
(2) Close the lock. (Score correct if patient attempts task.)
(3) Where is the key?
(4) Which one do you eat with?
(5) Which pencil is longer?
(6) Put the spoon in the cup.
(7) Put the cup beside the spoon.
(8) Close the lock and ring the bell.
(9) Put the bell between the pencil and the spoon.
(10) Point to the cup, the pencil, and the key.

b. *Following a paragraph* *Number of Errors:*

(May be omitted if patient makes errors on Test 3.)

Say: *I am going to read you a story. When I finish, I will ask you some questions about it. Don't try to remember it word for word, just listen for the story. Are you ready?*

Gold was first discovered in California by a millwright named James Marshall. Marshall was building a sawmill on the banks of the American River. One morning in January 1848, Marshall was walking along the millrace when he saw some bright flakes at the bottom of a ditch. He picked up a handful and took them back to the fort to show his partner, John Sutter. They turned out to be pure gold. Marshall and Sutter tried to keep the discovery a secret until the mill was finished, but the news spread like wildfire. Every morning goldseekers, armed with picks and shovels, came to the sawmill. Marshall sent them off in all directions, telling them better places to look for gold. To his surprise, they found it, and Marshall soon gained such a reputation that people would dig anywhere he suggested. No one had any idea that the whole countryside was one great bed of gold.

Questions

(1) Did Marshall discover gold in the Yukon?
(2) Did he find it at the bottom of a ditch?
(3) Did Marshall and Sutter spread the news of the discovery?
(4) Did many prospectors come to the sawmill?
(5) Did they tear down the sawmill?
(6) Did Marshall know where the hidden deposits were?

SECTION B
READING DISTURBANCES

1. *Word Recognition* (Visual) *Number of Errors:*

Materials: Card 1, Card Series 1A.

Place Card 1 in front of patient. Hold up first printed word and say: *Show me this, on the card.* Continue in order given below.

(1) car	(3) table	(5) house
(2) clock	(4) chair	(6) bed

2. *Word Recognition* (Auditory) *Number of Errors:*

Materials: Card 2A.

Place Card 2A in front of the patient. Say, *Show me dog.* Continue in order given below.

(1) dog	(3) tree	(5) horse
(2) girl	(4) flower	(6) boy

3. *Reading Comprehension* *Number of Errors:*

a. *Reading sentences*

Read first sample sentence aloud to patient, then, pointing to *yes* and *no*, ask: *Which is the right answer?* If patient makes error, say: *Christmas is in December, isn't it? So the answer is yes. Mark it here.* Follow same procedure with second sentence. If the patient makes an error, say: *No, you don't row a boot; you row a boat. The answer is no. Mark it here.* When the patient understands, say: *Now, you do the others the same way.*

Sample Sentences

Is Christmas in December?	Yes ( ) No ( )
Do you row a boot?	Yes ( ) No ( )
(1) Are there seven days in a week?	Yes ( ) No ( )
(2) Does milk come from crows?	Yes ( ) No ( )
(3) Does the sun rise in the east?	Yes ( ) No ( )
(4) Do you tell time with a match?	Yes ( ) No ( )
(5) Do all children like to go to school?	Yes ( ) No ( )
(6) Does everyone put money in the bank?	Yes ( ) No ( )

b. *Reading paragraph* *Number of Errors:*

(May be omitted if patient makes errors on Test 3.)

Say: *Read the paragraph, then read the questions and mark the right answers. You may go back and reread if you want to.*

Lawrence Griswold, a writer and scientist who lives in Minnesota, states that dragons really exist. In 1934 he

and a classmate camped for eight months on Komodo, an island in Indonesia. Here they found dragons 18 feet long, who walked on their hind feet like the ancient dinosaurs. They lived in mountain caves and came down to prey upon animals and people in the lowlands. Griswold and his companion trapped 43 of these strange creatures. He reported they were disagreeable reptiles with bad tempers, who hissed when they were angry. Griswold brought four of them back to the United States. One died during the voyage. Two were sold to the Bronx Zoo, and one to the Smithsonian Institute.

Questions

(1) Did Griswold find dragons in Indonesia? Yes ( ) No ( )
(2) Did they prey upon people? Yes ( ) No ( )
(3) Did the dragons live in caves in the sea? Yes ( ) No ( )
(4) Did Griswold find any dinosaurs? Yes ( ) No ( )
(5) Does Griswold think dragons are imaginary? Yes ( ) No ( )

SECTION C

SPEECH AND LANGUAGE DISTURBANCES

1. *Cranial Nerve Involvement* *Number of Errors:*

Materials: Flashlight, watch with second hand. Demonstrate what you want the patient to do; ask him to imitate.

(1) Say *ah*, five times. Score error if patient *cannot initiate phonation.*
(2) Say *ah*, prolong. Score error if patient *cannot sustain phonation 5 seconds.*
(3) Protrude tongue. Score error if *tongue deviates from midline at rest.*
(4) Move tongue from left to right corner of lips. Score error if *lateral movements are unequal.*
(5) Open mouth wide. Observe uvula with flashlight. Score error if *uvula deviates from midline at rest.*
(6) Say *ah* five times; observe with flashlight. Score error if *movements of two sides of soft palate are unequal on phonation.*
(7) Say *ah* five times; observe with flashlight. Score error if *palate is not elevated on phonation.*
(8) Score error if patient reports *difficulty swallowing.* Verify report.

2. *Sensorimotor Involvement* *Number of Errors:*

Say: *I want you to listen, and repeat the word I say. I will say each word twice, then you say it.* Say word distinctly, pause, then repeat and wait for patient's response. Score any mispronunciation as an error. Listen for initial consonant.

Lips: (1) pie, (2) boy, (3) me, (4) foe, (5) vow. *Tongue:* (6) toe, (7) day, (8) no, (9) lie, (10) row, (11) they, (12) yes. *Palate:* (13) key, (14) go. *Complex Coordinations:* (15) see, (16) shoe, (17) joy, (18) chew, (19) split, (20) spry, (21) street, (22) screw.

3. *Naming* (Auditory Recall) *Number of Errors:*

Materials: Cards 1 and 2.

Present Card 1. Point to the car and say: *What is this?* Continue in order given. Use same procedure with Card 2.

(1) car	(4) chair	(7) dog	(10) flower
(2) clock	(5) house	(8) girl	(11) horse
(3) table	(6) bed	(9) tree	(12) boy

4. *Functional Speech*

a. *Definitions* *Number of Errors:*

(May be omitted if patient makes errors on Test 3.)

Say: *What does robin mean?* If patient hesitates, say, *Just tell me in your own words. What is a robin?* If response is incomplete, say: *Can you tell me any more?* Record responses.

The object is not to find out if the patient knows what the word means, since these are all common words, but to determine whether or not he has enough language to explain a familiar concept. A definition does not need to be literary to be scored correct, but it should explain what the word means, and not merely give a common association. Examples are merely illustrations, not required answers.

(1) robin
Correct: bird.
Incorrect: robin redbreast.
(2) island
Correct: land surrounded by water.
Incorrect: wavy shore line; Long Island
(3) motor
Correct: something you use for power. drives a car or a boat. engine.
Incorrect: motor boat. in a car.
(4) bargain
Correct: a good buy. you get something at a good price.
Incorrect: bargain sale (Question).
it's a good bargain.
(5) courage
Correct: you keep on going. (Question). you're in a tough spot and you keep on going, you've got courage.
Incorrect: maybe you've got courage and maybe you haven't. (Question). don't know.
(6) repair
Correct: you fix something. make it go.
Incorrect: repair a tire. (Question). don't know.
(7) leather
Correct: skin from animals.
Incorrect: shoe leather (Question). cloth.

b. *Proverbs* *Number of Errors:*

(May be omitted if patient makes errors on Test 4.)

Say: *I am going to give you an old saying, and I want you to tell me what it means. For example, there is an old saying that goes, don't cross the bridge before you come to it. It means you shouldn't worry about things before they happen, because they might not happen at all. Now what does this one mean?* Item is not scored correct unless a general application is made.

(1) Don't put all your eggs in one basket.
(2) Don't count your chickens before they are hatched.
(3) Don't change horses in the middle of the stream.

SECTION D

VISUAL AND WRITING DISTURBANCES

1. *Revisualization*

a. *Draw a man* *Number of Errors:*

Give patient a clean sheet of paper. Say, *Now will you draw a man? It doesn't have to be artistic. Just draw it as well as you can.* If patient stops after drawing head, say, *Now draw the rest of him.* If patient begins to draw a very tiny figure, stop him and say, *Make it bigger.*

Score 2 errors if part is missing or grossly distorted (eyes outside head, arms or legs not attached to trunk, etc.). Score 1 error if part is distorted or slightly misplaced although in correct relation to the figure. If figure is drawn in profile, do not score error if second eye, arm, or leg is not shown. Score the following:

(1) head	(5) trunk
(2) eyes(2)	(6) arms(2)
(3) nose	(7) legs(2)
(4) mouth	

b. *Reproducing symbols* *Number of Errors:*

Say: *Now I am going to show you some letters. When I hold up the card, look at the letter, then*

print it just as you see it. Some of the letters are capitals, others are not. Be sure to make the letter just the way it is on the card. Expose each card 2 seconds, and remove it before patient writes. Encircle errors.

W N V M	B K P R H	t p d f b
L J F E	G Q D C	u n r h

2. *Spelling*

a. *Written* *Number of Errors:*

Pronounce word, read phrase, pause; say *write man*, et cetera. No further repetition is permissible.

(1) Man: an old man: write *man.*
(2) Has: he has a car: write *has.*
(3) Rain: it looks like rain: write *rain.*
(4) Watch: my watch is slow: write *watch.*
(5) Yellow: the leaves are yellow: write *yellow.*
(6) Business: business is good: write *business.*

b. *Oral* *Number of Errors:*

Remove paper. Say: *Now will you spell the same words aloud? Spell man.* Examples need not be repeated unless patient is unsure of word.

(1) man	(3) rain	(5) yellow
(2) has	(4) watch	(6) business

3. *Functional Writing*

a. *Sentences to dictation* *Number of Errors:*

Say: *Now I want you to write some sentences. I will read each sentence only once, so listen carefully. Are you ready?* Each sentence is read as a unit. A sentence is scored wrong if it contains an error in spelling or wording.

(1) The grass is green.
(2) We have a new car.
(3) There was a storm last night.
(4) Do you think it will rain today?
(5) The farm is about thirty-five miles north of here.
(6) I want a loaf of bread, a pound of sugar, and a dozen eggs.

b. *Spontaneous writing* *Number of Errors:*

Materials: Card 3.

Say: *I want you to write a paragraph about this picture. Describe the picture and tell what is happening. Write as much as you can. I will tell you when to stop.*

Stop the patient at the end of five minutes from the time he has actually begun to write. Count each of the following as an error:

(1) Produces less than 45 words in 5 minutes.
(2) Contains confused and irrelevant statements.
(3) Incorrect word usage.
(4) Defective sentence formulation.
(5) More than five errors in spelling, essential punctuation, or capitalization.
(6) Enumeration only.

TEST MATERIALS

1. Cut out materials and mount on cards for ease of administration. Each letter should be on a separate card and presented individually.

2. In addition to the printed materials, the following objects are necessary: stopwatch, or watch with second hand, pad of paper and sharpened pencils, flashlight, bell, cup, padlock and key, a long and a short pencil, and a spoon.

Test materials prepared by Medical Illustration Service, Minneapolis VA Hospital, Lawrence B. Benson, artist.

■ It is evident that the whole nervous system is double; but the phenomena of disease show that damage to *one* hemisphere (usually the left) will produce loss of speech, and that damage to *one* hemisphere (usually the right) will not produce loss of speech.

Right-handedness is further evidence that the two halves of the nervous system are different. It seems, then, that the two halves are not mere duplicates; neither are they two juxtaposed singles. A careful study of cases of disease of the nervous system has led me to conclude that *each* side of the brain contains processes for all classes of movements of both sides of the body, but that it contains them differently. The phenomena of hemi-spasm show that the muscles of *both* sides: (1) those which must act bilaterally; (2) those which may act alternately; and (3) those which can act independently—are all represented in *each* side of the brain.

J. Hughlings Jackson in *Notes on the Physiology and Pathology of the Nervous System,* published in 1868.

Digital Carotid Artery Compression with Occlusion of the Anterior Cerebral Artery

E. S. Gurdjian M.D. and J. E. Webster, M.D.

IN THE COURSE of investigation of patients presenting clinical evidence of cerebrovascular disease, angiography has revealed instances of occlusion of one anterior cerebral artery. Invariably, when the anterior cerebral did not fill on ipsilateral injection of media, filling resulted from contralateral injection. The term occlusion is used in this paper to describe an anatomic abnormality or thrombosis of the proximal portion of the anterior cerebral artery.

It was noted that, when one anterior cerebral artery was occluded, contralateral digital carotid compression resulted in profound syncope attended with convulsive movements. The importance of these forebrain arteries in serving consciousness was strikingly emphasized. This clinical observation has a basis also in anatomic studies, particularly those of Abbie.[1] This investigator, in studies on the forebrain arteries in many phyla of animals, has reported the anterior cerebral arteries as a primitively vital structure. The principle of vascular constancy of pattern in the blood supply to the brain in evolution supports the concept of the continuing important role of the anterior cerebral arteries in man as well as animals.

A study of ten patients with anterior cerebral artery occlusion has been made, employing carotid compression tests in addition to routine neurologic studies, including angiography.

METHOD — DIGITAL CAROTID COMPRESSION

Digital compression of the cartotid bulb is applied carefully with the patient sitting upright upon an examining table or bed. An assistant notes the pulse while the carotid bulb is first gently palpated and then gradually compressed. A warning of beginning of syncope may be subjective symptoms of dizziness and blurred vision; slowing of the pulse may suggest a carotid sinus sensitivity. Loss of consciousness may be associated with convulsive movements of brief duration. At the first sign of syncope, the compression is released and the patient placed in the supine position. Simultaneous electrocardiogram, electroencephalogram, and blood pressure records may aid in evaluating the response. Examination of both fundi with light globe pressure at the time of the compression and ophthalmodynamometer tests may also be used. Having been performed in hundreds of patients, this carotid compression test has not proved dangerous but it must be used cautiously.

RESULTS

Table I is a summary of the ten cases in this study. Seven presented right and three left anterior cerebral occlusions. Improper filling of the anterior cerebral artery may occur in angiographic studies, but such patients have no syncope upon contralateral compression and a repeated angiogram may be normal. Congenital abnormalities of the anterior cerebral artery may also result in the diagnosis of an occlusion based upon the angiographic pattern of nonvisualization.

The patients with occlusion of the proximal portion of the anterior cerebral artery may have neurotic manifestations with some motor deficits. Contralateral hemiparesis or monoparesis was seen in five instances. In one case there was a history of attacks of numbness of the ipsilateral half of the body.

COMMENT

The pathophysiologic effects of anterior cerebral artery occlusion have been of considerable practical interest to neurosurgeons who have encountered these vessels surgically in dealing with contiguous neoplasms or, more recently, aneurysms. It was thought for some years that ligation or thrombosis of the dominant anterior cerebral artery may be followed by profound unconsciousness due to damage to the anterior part of the corpus striatum. Dandy's[2] original observation and supplementary report in this regard have been rejected by Meyers,[3] who has purposely damaged this area in Parkinson operations (24 cases) without resulting unconsciousness (in one patient a bilateral operation was done). We have encountered two patients, both of whom were conscious following ligation of both anterior cerebral arteries proximal to the communicating artery necessitated during the removal of saccular aneurysms involving the anterior com-

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TABLE 1

Case	Age	Sex	Angiogram	Neurostatus	Compression
1.	33	M	Occlusion of rt. ant. cerebral—fills from lt.	Tense, nervous, considered psychiatric problem. No neurologic findings	Lt.—syncope; Rt.—0
2.	63	F	Occlusion of rt. ant. cerebral—distal portion fills from lt.—(angiogram checked 4 week intervals)	Tense, nervous, mild lt. arm weakness, personality disturbance	Lt.—syncope; Rt.—0
3.	70	M	Occlusion of rt. ant. cerebral—fills from lt.	Weakness of rt. arm and both legs—confusion, generalized weakness (died)	Lt.—syncope; Rt.—0
4.	40	F	Occlusion of rt. ant. cerebral—fills from rt.	Generalized weakness, disoriented, weight loss	Lt.—syncope; Rt.—0
5.	53	M	Occlusion of lt. ant. cerebral—fills from rt.	Aphasia, rt. hemiparesis, generalized weakness (recovery)	Lt.—0; Rt.—syncope; Negative exploration as brain tumor
6.	39	M	Occlusion of lt. ant. cerebral—fills from rt. (rechecked angiogram)	Numbness and weakness of rt. side of face, arm, and leg (recurrent)	Lt.—0; Rt.—syncope
7.	59	M	Occlusion of lt. ant. cerebral—fills from rt.	Headache, confusion, disorientation, rt. hemiparesis, dizziness, hazy, weakness, generalized	Lt.—0; Rt.—syncope; Explored for subdural hematoma
8.	47	M	Occlusion of rt. ant. cerebral—fills from lt.	Nervousness, personality defect (improved)	Lt.—syncope; Rt.—0; (Lt. subdural abscess—previously)
9.	37	M	Occlusion of rt. ant. cerebral—fills from lt.	Headache, dizziness (marked) generalized weakness	Lt.—near syncope; Rt.—0; Lt.—blurred vision and increased dizziness
10.	63	M	Occlusion of rt. ant. cerebral—fills from lt.	Dizziness, mild weakness of rt. arm (improved)	Lt.—syncope; Rt.—0

municating artery. One of these patients developed a hyperosmolarity syndrome which she fortunately survived. We restated,[4] in reporting these patients, that the blood flow available from the middle cerebral arteries (as proposed by Dandy) probably accounted for adequate collateral flow to maintain consciousness and life in these two instances. Heubner's artery or multiple small nutrient arteries termed "anterostriate" may arise from the middle cerebral artery in one-fourth to one-third of cases, according to Dandy.

When one anterior cerebral artery is occluded proximal to the anterior communicating artery (and if the occlusion is not an artifact), the possibility of unilateral occlusion of Heubner's artery (medial striate) and the adjacent "anterostriate" vessels with brain ischemia or infarction exists. The anterior cerebral artery may still fill with contrast media and appear normal at and above the communicating artery upon contralateral injection. (It is of note that thus far in no patient have we encountered an absence of both anterior cerebral arteries except in those surgically ligated, nor has Ecker.[5])

Under these circumstances, when the blood flow to the functioning contralateral anterior cerebral artery is temporarily reduced by contralateral digital carotid compression as described, unconsciousness usually occurs promptly, with associated characteristic clonic convulsive movements. The fundus on the side compressed may pale as the retinal arterial flow reduces and the pressure falls, as demonstrated by the ophthalmodynamometer. The temporarily induced unconsciousness thus suggests a relationship to the frequently irreversible state which has been encountered by the permanent occlusion of both vessels.

The development of syncope suggests two pathophysiologic possibilities: one, that the area of the brain supplied by Heubner's artery (medial striate) and the "anterostriate" arteries may be among areas strategic in maintaining consciousness; the second, that a major quantity of blood flow to the entire brainstem is critically reduced. Flow to the brainstem is the net result of supply from the carotid and vertebral systems and is dependent upon their patency, as well as the anatomic variations and patency of their branches composing the circle of Willis. When consciousness is acutely influenced (manifested by syncope) due to carotid compression, there has resulted a reduction in total blood flow to the brain. In some patients the contribution of flow from both anterior cerebral arteries may be necessary to maintain a basic total flow toward maintaining consciousness. However, it is of interest that when the middle cerebral artery trunk is occluded rather than the anterior, con-

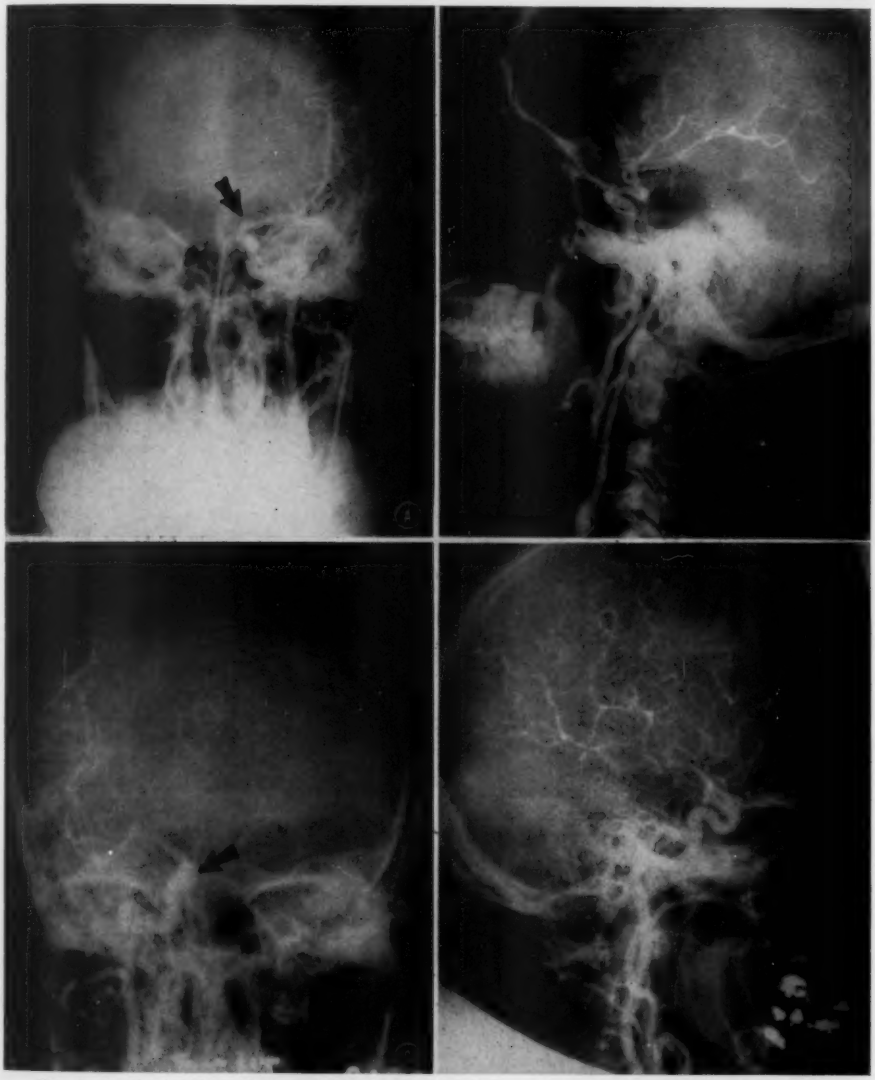

FIG. 1. *A* and *B*. Anteroposterior and lateral views of angiogram in case 6. Left anterior cerebral is not demonstrable. This patient has made an almost complete recovery. *C* and *D*. Anteroposterior and lateral views of the right carotid distribution. No neurologic findings. Patient has been considered to be a psychiatric problem.

tralateral carotid compression does not result in syncope in the great majority of patients. The contribution of the anterior cerebral flow seems, therefore, related more directly to the function of centers controlling consciousness.

A congenitally small or absent anterior cerebral artery with a normal or enlarged contralateral vessel may result in signs and symptoms, with aging, of insufficiency, with eventual inadequacy of the channels in the distri-

bution of medial striates on the same side as the congenital abnormality. In case 3 the anterior cerebral artery was extremely small on the right. The right posterior communicating artery was hair-like. The compression of the left carotid resulted in syncope. The left anterior cerebral was enlarged; the anterior communicating was also unusually well formed, with large vessels to both hemispheres found in the supracallosal and callosomarginal distributions.

The question arises concerning the time of onset of the clinical evidence of insufficiency in such patients. It is possible that insufficiency was present early in life; however, with atheromatous changes occurring due to aging (72 years of age), cerebrovascular failure may then occur eventually in the distribution of the proximal portion of the left anterior cerebral artery. Such failure would seem to be related to the anatomically abnormal anterior cerebral and posterior communicating vessels. In an emergency, these vessels cannot contribute to the needed collateral circulation. Blackburn[6] has reported a high percentage of such abnormalities among patients in an insane asylum.

Abbie[1] studied the principle of vascular constancy in the brain from fish to man, including amphibia, reptiles, and mammals. Forty human brains were studied. In the dissections the arterial branches were followed individually to their destinations with the aid of a binocular microscope. The reptilian brain first showed a differentiation into three major channels, the anterior, middle, and posterior cerebral arteries. The anterior cerebral artery represented the medial olfactory artery of the lower forms. The middle cerebral artery appeared as an entity for the first time in reptiles. The gap between reptile and mammal is characterized by the development of the cerebrum. The middle cerebral artery enlarged to meet this mammalian need. However, the anterior cerebral artery is the most primitive artery of the brain related to primitive consciousness.

Studies of the forebrain arteries in man have also been made by others.[7–17] Kaplan and coworkers[18] stated that "the anterior cerebral artery near its origin gives off branches to the most anterior portion of the hypothalamus and slightly more distally the artery of Heubner which enters the anterior-inferior caudate head and after traversing the anterior-inferior portion of the internal capsule terminates in the antero-infero-mesial region of the putamen."

For many years the basis for clinical neurologic speculations has been based upon information presented by Duret[7] (1872-74), a student who did anatomic work for Charcot*[18] at the Salpetriere. Duret's findings have not been confirmed by others, although distorted illustrations of his descriptions by Charcot's artist, M. Claivault, still appear in neurologic texts.

In the same year that Duret's work was published, Heubner[8] of the University of Leipzig reported a "recurrent" artery as an important branch of the anterior cerebral artery found constantly on both sides in the 30 brains studied. This pattern of vascularity has been confirmed,[1,10,17] although it is seldom portrayed or considered in neuroanatomy and neuropathology. The role of this vessel in supplying ganglionic structures may pertain to neurologic states involving consciousness and neurologic disability.

The definition of clinical signs and symptoms of anterior cerebral artery occlusion was established in considerable detail by Critchley[19] in 1930. A review of his clinical and pathologic data in the light of our present knowledge must question the accuracy of his conclusions, which have been widely accepted previously. The first case (of seven cases reported) cited by Critchley, illustrating the clinical result of an occlusion of the main trunk of one anterior cerebral artery, was that of a 95 year old asylum inmate with senile dementia and "wide spread sclerosis of the cerebral vessels." Since the cervical carotid bulb areas in these patients were not evaluated, this case, as well as others providing evidence for a characteristic anterior cerebral artery syndrome, may not now be validated. Early clinical correlations have been based upon "false" and "delusive" pathologic investigations,[20] as well as the inaccurate anatomic observations of Duret.

As may be seen in table 1, there is a variability of symptoms and signs in the presence of occlusion of the proximal portion of the anterior cerebral artery. This is because collateral blood flow may vary in each patient. Such collateral flow may be excellent in the convexity branches of an anterior cerebral artery. Collateral flow may also occur in the basal or ganglionic branches, but this depends upon the patency and anatomy of the carotid and

*Charcot stated: "The anterior cerebral artery has very modest attributes—it arterializes only the head of the caudate ganglion and even in this its participation is not constant."

FIG. 2. *A* and *B*. Right and left carotid angiograms showing no filling of right anterior cerebral but bilateral filling of anterior cerebrals from the left side. No neurologic abnormalities, but severe headaches, dizziness, generalized weakness (case 9). *C* and *D*. Right and left carotid angiograms in a patient with weakness of right arm and both legs and confusion. Autopsy showed a very small anterior cerebral (non-functioning) artery (case 3).

vertebral systems and their branches in the Circle of Willis.

It has seemed possible to us that unilateral occlusions of the medial striate or ganglionic branches of an anterior cerebral artery associated with ischemia in the area of its supply may be attended by "psychosomatic" symptoms. We have noted that symptoms such as

nervousness, fear, insecurity, dizziness, "faint-like spells," and particularly generalized weakness and "weak spells" are common in these patients (table 1). Such symptomatology recalls the statement made by Hughlings Jackson[21] in 1874 that "I confess I think it will turn out that the pathology of the neurosis is in most cases owing to arterial disease." When the main trunk of the anterior cerebral artery is occluded and if collateral circulation is insufficient, ischemia of the foremost half of the anterior limb of the internal capsule and the medial portions of the frontal and parietal lobes may account for varying degrees of hemiplegic and hemiparetic states as well as the above symptoms.

SUMMARY

It has been noted that patients with an occlusion of one anterior cerebral artery proximal to the anterior communicating artery may develop syncope upon contralateral digital carotid artery compression.

Blood flow from both anterior cerebral arteries seems necessary to preserve consciousness, because of the contribution of these vessels to the total blood flow of brainstem and hypothalamic centers.

The patency of the carotid and vertebral systems, the Circle of Willis, and the collateral circulation available determine the pattern of neurologic deficits when an anterior cerebral artery is occluded, either proximal or distal to the anterior communicating artery. Such an occlusion may result in cerebrovascular failure. Previous neurologic concepts must be revised on this basis.

In the patients with anterior cerebral artery occlusion reported in this paper, the psychosomatic symptoms were outstanding, including nervousness, generalized weakness, and "faint-like" spells. In some cases contralateral hemiparesis or monoparesis coexisted with the nervous symptoms.

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■ Galen considers the brain as the grand organ of intellect. The rational soul dwells in the brain, he says, and by it we reason.

It is by the nerves, he says, we have sensation and voluntary motion; and it is reasonable that we should place the soul, the presiding principle, which acts by means of them, at their origin: but the origin of the nerves is in the brain, therefore the governing principle is in the brain.

John Cooke in *A Treatise on Nervous Diseases*, published in 1824.

Definitions of Cerebral Palsy and Their Role in Epidemiologic Research*

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THE INCIDENCE of cerebral palsy in the resident population of Rochester, Minnesota, as described later in this paper, has been found to be considerably less than that reported in other statistical surveys in the United States. It was felt that this discrepancy was due, not to inadequate case finding, but to the use of a specific definition in the Rochester[1] survey, in contrast to the vagueness or absence of any definition of cerebral palsy in the other surveys. In this paper, the definitions of cerebral palsy will be reviewed in the light of present epidemiologic concepts and reported statistical surveys; the definition and results of the Rochester survey will also be presented.

The epidemiologic approach, through field and statistical study, evaluates disease as it occurs in groups of people and compares features of the sick population with those of the well population. If the disorder under study can be properly defined and if the affected individuals can be identified, it may be possible to obtain a true picture of the occurrence of the disease and to delineate significant variations in time or place which may direct investigations of causative factors.

In epidemiologic research, a case of a disease entity in a given population represents the desired tabulation unit. If the disorder is not a disease entity, the clinical syndrome or symptom-complex must be defined as clearly as possible, if one expects to group those cases which, by correlation studies, may be found to be related etiologically.

UNIFORMITY OF DEFINITION AND METHOD

Dorn,[2] in emphasizing the need for unequivocal definition of illness in the application of biometric methods, has stated: "Statistics of ill-defined, unique, or dissimilar events (or ailments) are not only meaningless but may also be misleading." Recently Altman,[3] on reviewing several statistical reports, commented on "the lack of clear definition of what cerebral palsy is and the paucity of data about it." Many expensive and time-consuming surveys on the frequency of cerebral palsy in populations have been conducted, and potentially valuable information for further research may have been lost because of the failure to define clearly the methods used or the disorder being measured.

How carefully one defines cerebral palsy is in part determined by the use one intends to make of the term. The definition for the activities by a voluntary agency or for a legislative hearing must be clearly stated in terms that laymen will understand; it may also be sufficiently inclusive or diffuse to attract the greatest possible interest and public support. But this same definition may not be appropriate in a medical research protocol. For the latter purpose, it is basic to scientific method to define the disorder that one intends to measure as specifically as our present diagnostic knowledge and facilities allow.

The hazard of non-uniformity of definition and method becomes clearly exposed and the consequent vagueness and confusion become evident, if we examine, for example, a few of the reports which have been published in the past few years on the prevalence of cerebral palsy in various parts of the United States and in several European countries. The details of method are presented in appendix A; the estimated prevalence and incidence in these studies are presented in tables 1 and 2.

It is safe to say that no two surveys reviewed here have been conducted in the same fashion, that in none are the same sources of case finding used to the same extent, and that, in all previous surveys with which the author is acquainted, cerebral palsy either is not defined or is defined so broadly that the investigator's individual standards govern what was included as a case.

Various medical specialists have directed or participated in the surveys, and it is conceivable that this too has influenced the comparability of the cases collected. In most studies in the United States, orthopedists examined some of the patients; in a small study in Georgia (table 1), a neurologist was a member of the medical survey team. The European studies were directed by pediatricians with special interests in the cerebral palsy problem.

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In spite of these shortcomings, statements have been made suggesting that differences in race or obstetric care may account for the reported differences in prevalence. The possibility that methodologic differences might account, even in part, for the discrepancies in rates has usually been overlooked. A few examples will be presented to illustrate the need for restraint in concluding that differences in prevalence must have some etiologic basis, unless precautions have been taken to avoid the various hazards of nonuniformity.

DEFINITIONS USED IN FIELD STUDIES

In surveys in which a definition of cerebral palsy has been stated, the definition of Phelps or some modification thereof is used. Phelps[4] defined cerebral palsy as *"a group of conditions which affect the control of the voluntary motor system and have their origin in lesions of various parts of the brain."*

Let us reflect for a moment on this definition, which is basic in so many of the surveys. Note that the only limitations are *voluntary motor system* and *various parts of the brain.* This means that progressive or nonprogressive diseases of a developmental, traumatic, neoplastic, vascular, or infectious nature could be included. These might range from agenesis of parts of the brain of the newborn infant to paralysis agitans or even stroke in the aged.

Phelps[4] classified types of cerebral palsy into 1) those affecting the cortex, 2) those affecting the basal ganglia, 3) the ataxias (cerebellar), 4) the tremors, and 5) the "rigidities." (These five groups, incidentally, are not mutually exclusive.) He stated that "the fourth group is the small group‡ who have tremors which would include in older people such conditions as paralysis agitans, since paralysis agitans is a motor disability, the origin of which lies in damage to a certain part of the brain."

Although the definition of cerebral palsy, where given, is essentially that of Phelps, it is clear that some limitations, such as age at which brain disease developed, were incorporated in the surveys, since almost all patients were children or adolescents. It is evident that, in several of these surveys, some disorders were included that many neurologists would classify otherwise. For example, one of the few cases which were described in the statewide study in Connecticut[5] was that of a patient whose motor dysfunction was associated with hydrocephalus and spina bifida. Several patients described in the Birmingham, England, study[6] were children who had hydrocephalus or who had progressive degenerative spastic paralysis.

Andersen,[7] in his survey of Østfold County, Norway, was one of the few who modified Phelps's definition. Andersen stated that the definition of cerebral palsy on which he based his survey "does not include progressive lesions of the brain (or lesions of the spinal cord or peripheral nerves) . . . It is obvious that a brain lesion will seldom affect the motor centers selectively. Several centers will usually be involved simultaneously. Thus, the picture will be that of a motor lesion combined with various other defects, such as mental defects, epilepsy, visual and auditory disorders, etc."

Asher and Schonell,[6] in their study in Birmingham, England, did not define cerebral palsy, even though they listed the cases as congenital or acquired cerebral palsy.§ The congenital form was subdivided into symptomatic types (spastic, athetotic, ataxic, and so forth) and the acquired type was subdivided by presumed etiology or clinical type.

In all the surveys except that in Rochester, Minnesota, cases were similarly divided into "congenital" and "acquired" cerebral palsy.

The "acquired" cerebral palsy accounted for 8 to 13 per cent of the cases and affected children or adolescents whose disability followed an obviously infectious or traumatic episode or in whom, after a period of normal growth, a degenerative process developed. In the Birmingham, England, study, kernicterus is included in the "acquired" group, whereas in the others it is included in the "congenital" group.

OTHER DEFINITIONS OF CEREBRAL PALSY

If statistical studies on geographic distribution and differential incidence of cerebral palsy are to be of value, one must arrive at a definition of cerebral palsy that can be followed in surveys of different populations. Although Phelps and others directing community surveys have defined cerebral palsy very broadly, with no restriction as to age, such a limitation, and perhaps many clinical limitations as well, have probably been employed in the surveys them-

‡Parkinsonism is not "small" but is probably even more prevalent in the general population than cerebral palsy when "cerebral palsy" is defined as perinatal brain disease according to the limitations expressed later.

§Benda[8] and others have pointed out that the division into "congenital" and "acquired" is misleading and confusing. Reed[9] has expressed this as follows: "The failure to put one's birth in its proper perspective has led to no end of misconceptions as to the role of heredity. Many people have had the mistaken concept that diseases present before birth are hereditary and that those appearing post partum are not. Actually, the fleeting moment of birth is of small consequence in the long periods of development of diseases with hereditary backgrounds."

selves. We might explore further other definitions to see if one that might be useful for field studies is available or can be developed.

Perlstein's definition¶[10] is about as all-inclusive as that of Phelps. In effect, both say that any motor disorder of the brain occurring at any time is cerebral palsy. On the other hand, Courville••[11] has suggested that conditions such as cerebral vascular accident of the aged and other disorders occurring after the brain has fully developed should not be included. Crothers††[12] has limited the conditions included to children whose brain damage occurs prior to age three, and Benda‡‡[8] mentioned a limit of early infancy. Merritt[13] stated that cerebral palsy is a "heterogeneous group of cases with damage to the nervous system *in utero*, at birth, or early life" and "not a disease entity."

Denhoff and associates[14] and Cruickshank and Raus[15] pointed out that the problem of cerebral palsy is so complex that three types of definitions—that is, a "standard," a "practical," and a "limited" definition—would appear to have a place in clarifying different aspects of research or medical care matters. Definitions, such as that of Perlstein or Phelps, in which the disorder is defined "in terms of its physical components" are referred to as the *standard* type of definition. The *practical* definition is one in which cerebral palsy is viewed as one component of a broader brain damage syndrome, which would include motor, sensory, and psychologic dysfunction, convulsions, and behavior disorders of organic origin. These are "practical" in the sense that brain-damaged individuals with a variety of clinical dysfunctions have need for similar diagnostic and rehabilitation services and that, in terms of public education, cerebral palsy should not be limited to selected motor dysfunction. Neither the *standard* nor the *practical*§§ definition can be applied soundly in retrospective epidemiologic research; instead, a specific or *limited* definition will have to be adopted in spite of disapproval for the limited definition by the foregoing authors.

GOAL OF THE UNIFORM DEFINITION

One goal of the statistical studies on cerebral palsy is to clarify the etiologic mechanisms of a group of cerebral motor disorders in which some causes are suspected but most are unknown. For the epidemiologist, the group should have clinical features in common which insure the identification, by uniform survey methods, of the bulk of patients in a specified population. If this is successful, sound correlation studies of such patient "populations" and unaffected "controls" may suggest some etiologic associations and give direction to definitive studies of the individual disease entities which comprise the heterogeneous group.

DEFINITION DEVELOPED FOR THE ROCHESTER SURVEY

Since the interpretation of "cerebral palsy" is so vague, one may wonder if there is any value in retaining the term at all. It is believed that many of the cases included in the general concept of this term do have some etiologic bases in common, and that by merely providing more specific limits the term may be used to advantage. Therefore, the term "cerebral palsy" was retained and the notion that motor disability must be present was also accepted. In view of the fact that motor function is so widely represented in the brain, many types of brain injury¶¶ will be included. It is recognized that more than the motor system may be affected and that in some instances of brain injury which are excluded (for example, mental retardation without motor dysfunction), the same etiologic mechanism may have acted as in cases with pure motor disability.

For the purpose of statistical comparisons, it is desirable that the cerebral palsy category be as homogeneous as possible, even though that "homogeneity" may still represent a mis-

¶"Cerebral palsy is a condition characterized by paralysis, weakness or incoordination, or any other aberration of motor function due to pathologic involvement of the motor control centers of the brain."

••"Cerebral palsy obviously implies a paralytic state resulting from cerebral damage of any nature. Common usage has suggested that the term applies essentially to those cases in which the paralysis exists from birth or at least early life from causes acting on the developing brain."

††"A child has cerebral palsy when it has suffered injury of the brain occurring during the period of rapid development from conception to three years, which distorts orderly development and leads to abnormal motor control."

‡‡"Cerebral palsy denotes all those conditions in which interference with the control of the motor system arises as a result of lesions within the brain. It is obvious that the term includes a great variety of conditions. Since practically all expressions of human behavior are hinged upon the motor system, any interference with these expressions, from stammering to complete diplegia, could theoretically be included in the category of cerebral palsy. The term, however, is, at least traditionally, limited to conditions which go back to the beginning of life or early infancy and does not include injuries to the spinal cord."

§§In some respects, the practical definition is similar to the concept, expressed by Lilienfeld and Parkhurst[16] and by others,[17,18] of a "continuum of reproductive casualty." This matter is discussed further below, when anterospective epidemiologic research methods will be considered.

¶¶" . . . 'injury' encompasses any harm to the tissue, and histochemical 'injuries' are as much a part of brain injuries as mechanical and physical traumata."[8]

cellaneous collection. The following groups are omitted from present consideration as "cerebral palsy": cases of cerebral damage of obvious origin, such as severe trauma or encephalitis occurring in a normally developing child after the neonatal period; progressive degenerations occurring in a normally developing child after the neonatal period; and the reasonably well-defined, fairly distinct neurologic disease entities or symptom complexes such as hydrocephalus or mongolism. This does not mean that such disorders are excluded from study, for, as seen in table 3, they were investigated separately in the surveys; it merely means that, after the specified groups were listed, the heterogeneous residue with motor dysfunction observed during infancy was classified as cerebral palsy.

In the hope of presenting a definition which might be adequate for uniform epidemiologic usage, the following definition of "cerebral palsy" is adopted in the present study: The term "cerebral palsy" refers to those disorders of uncertain or unknown etiology arising during the perinatal period—that is, from conception to the end of the neonatal (first month) period—affecting the motor function of the brain and in which the dysfunction is recognized prior to the end of infancy (two years). Disease entities such as congenital syphilis with resulting paralysis, those of a progressive nature such as tuberous sclerosis, Tay-Sachs cerebral-macular degeneration, or well-recognized symptom complexes which may affect motor function, such as hydrocephalus, mongolism, or encephalodysplasia, are not included in this cerebral palsy category.

It is felt that the exclusion of the other recognized symptom complexes and disease entities, which, if included, would have distorted the pertinent statistics, should provide a more reasonable point of departure for comparative epidemiologic research.

The diagnosis of cerebral palsy, according to this concept, becomes, first, a more limited but still a miscellaneous category and, second, essentially a diagnosis of exclusion. The diagnosis of a known disease entity, another distinct clinical syndrome, or the recognition of a toxic, traumatic, neoplastic, or infectious etiologic agent recognized as acting for the first time after the neonatal period is reason for exclusion from the category of cerebral palsy.

In adopting this definition, one must recognize that cases of perinatal brain injury occurring in fetal or neonatal life may not be recognized until early childhood and that, if brain injury or defect is severe enough to cause death in early infancy, the diagnosis of cerebral palsy will not be made. Thus, cerebral palsy is essentially a clinical diagnosis in which the most severe cases are eliminated by early death and in which the milder cases are also likely to remain undiagnosed and thus unreported for survey purposes.

The age at which the disease process develops or occurs is, presumably, between conception and the end of the neonatal period. The age at which a physical retardation may first be recognized will depend on the normal age of development of the activities which are affected. Thus, speech defects are usually recognized later than gross incoordination of the extremities; yet both might be due to the same mechanisms or cause in the same patient. In almost all cases, perinatal disease affecting coordinated motor activity will be recognized during infancy (that is, the first two years of life), and this time limitation is adopted here.*†

ESTIMATED FREQUENCY OF CEREBRAL PALSY

Methods of case finding. Birth incidence rates have been reported by Pohl[19] for Minneapolis, Minnesota, by Anderson[20] for Baltimore, Maryland, and by Ingram[21] for Edinburgh, Scotland. Prevalence, or the number living in the population, was estimated in many other surveys.

The most widely quoted figures on the frequency of cerebral palsy are those developed by Phelps, which were based on "repeated samplings done in New Jersey, Maryland, and other areas." Unfortunately, Phelps[22] has not published a report which describes his case finding methods or the statistical calculations on which his general statements on prevalence are based. The surveys in Connecticut[5] and the development of the case registers in Denmark,[23,24] Sweden,[25] Edinburgh, Scotland,[21] and Birmingham, England,[6] were made with varying degrees of thoroughness through many sources of medical information, including public health officials, practicing physicians, pediatric and orthopedic services of hospital registries, and welfare agencies. In the survey in Norway, there was also house to house can-

*In a sample of the cases in the Connecticut study,[5] parents had noted motor dysfunction before age two years in more than 90 per cent of cases (about 10 per cent of the cases in that study were "acquired" or so-called late-developing cerebral palsy).

†Although a parent may recognize or, in retrospect, consider a child as physically retarded before the end of infancy, medical care may not be sought until months or years later. Such cases would, of course, be included for survey purposes.

vassing by members of a women's welfare and public health association, which accounted for more than 25 per cent of the cases found. The surveys in Schenectady County, New York,[26] and in Georgia[27] included a publicity program, reports from physicians and institutions, and canvassing of samples of the population.

Results of surveys other than Rochester, Minnesota. Except for the survey reports of Phelps, which have attracted so much attention, the detailed comparisons of the methods and results are presented in appendix A for those studies which seem to warrant further consideration.

All of Phelps's reports are about as follows:

On the basis of statistics gathered through the last 20 years in various parts of the country in both urban and rural areas, it has been found that in every 100,000 population seven infants who have cerebral palsy are born each year (approximately seven per 1,500 births). Of these, one dies in infancy, or at least under six years of age, so that the real frequency for normal life expectancy is six new cases each year in every 100,000 population. This number (six per 100,000 per year) is constant and is the same in the mountains of West Virginia or Kentucky as it is in New York City or Detroit, for example.[28–30]

In regard to the six survivors per unit of population, Phelps made the implausible statement that "the mortality rate in these patients is no greater than normal."[4] The "rate" employed by Phelps is novel in the field of public health statistics and has been converted in table 1 to the more orthodox prevalence and birth incidence rates.‡

The rate reported by Phelps is equivalent to a prevalence rate of 400 per 100,000 population.[26] It appears either that Phelps's surveys were very incomplete or, more likely, that he did not follow his own definition or classification of cerebral palsy in these "repeated samplings" since, according to other studies, the prevalence of paralysis agitans alone is greater than 400 per 100,000 population.[1]

The Schenectady County results reveal a higher birth incidence than reported from any other source. The highest prevalence rate was reported for children of school age, the children who are most likely to be observed for physical defects and registered in medical and social agencies. In this study a sample of patients was examined by an orthopedist but the results of that examination were not reported.

In Connecticut no variation by county that seemed to be important was noted. Also, in this study it was suggested that the more severely disabled children are relatively overrepresented in the sample and milder cases are more likely to be missed; 75 per cent of cases were "moderate" or "severe." Twenty-four per cent of the children had convulsive disorders, and about 60 per cent were mentally retarded.

It was also noted that, in 97 of 103 children for whom the information was available, the parents had noted some disability within the first two years of life, although medical assistance was often not sought until later.

England, Scotland, Sweden, Norway, and Denmark. The prevalence and birth incidence rates reported from these countries vary somewhat, but are generally lower than those reported in the United States surveys (tables 1 and 2). Perlstein[10] has concluded from this that the frequency of cerebral palsy is lower in these European countries than in the United States. The European surveys, however, were of relatively limited scope as compared to that in Schenectady County, New York, and that in Connecticut. Nilsonne,[25] the author of the report from Sweden, has speculated that the rate in Sweden is lower than that of the United States because of differences in race or obstetric care. He failed to consider the possibility that the survey methods were so different as to make any such comparisons impractical.

In many of these retrospective studies an attempt was made to clarify the importance of such items as family history, maternal age, mother's health during pregnancy, birth order, sex incidence, incidence of prematurity, incidence of twins, history of obstetric complications, neonatal history, serologic signs of Rh incompatibility, and other factors. In the Connecticut study[5] and the study in England,[6] for example, histories of prematurity, difficult

‡Definitions: *Prevalence* of a disease may be defined as the number of cases per unit of population (usually 1,000 or 100,000) living on a given date. *Incidence* of a disease may be defined as the number of new cases which develop during a given period (usually a year) per unit of population.

Ordinarily, one attempts to relate numerator and denominator of a rate as closely as possible. A birth incidence, for example, could describe the number of children with a particular disorder per 1,000 births. Phelps's rate of six births per 100,000 population is a sort of specific birth rate, that is, the number of children who have cerebral palsy born per 100,000 population—the usual "birth rate" being the number of births per 100,000 population. To derive the number of cerebral palsy cases in the population at any time (prevalence), one must know the birth incidence, the birth rate, and the duration of illness. Since birth rates vary greatly with numerous factors, including age distribution, economic and social conditions in the population, and so forth, the type of "rate" presented by Phelps is difficult, not only to determine, but also to compare in different populations. It was converted to orthodox rates in the Schenectady County, New York, study.[26]

TABLE 1
ESTIMATES OF FREQUENCY OF CEREBRAL PALSY (U.S.A.)*

	Estimated or reported prevalence per 100,000 population				
	Total	Aged 5 to 9 years	Aged less than 20 years	Aged less than 21 years	Estimated birth incidence per 1,000 births
Selected areas (some undefined) (Phelps)	400†	400			4
Schenectady County, New York					
Before house to house canvass	90	440	223		
After house to house canvass	152	634	381		6
Connecticut study					
Before "correction factor" was applied		203		170	
After "correction factor" was applied		345		288	
Clarke and Oconee Counties, Georgia				500	
Minneapolis, Minnesota					1.8
Baltimore, Maryland					2.9
Rochester, Minnesota (present study)	70		160		0.6

*For sources of data, see appendix A.

†Assuming a normal life expectancy after age five years.

labor, Rh incompatibility, placenta previa, or a stormy neonatal period were said to be common in the cerebral palsy patients. The authors in the latter study also reported that, among the cerebral palsy patients, there were more first-borns, more twins, more children of older mothers, and more boys than would be expected in a random sample of the general population. Since, in many of the surveys reviewed, data of similar type from a comparable "normal" population are not available, the association may suggest, but frequently fails to give convincing support of, a cause-and-effect relationship.

Frequency by race and economic status. Variations by race or economic status are difficult to evaluate at present. According to Perlstein,[10,22] cerebral palsy is "more common among the white race than among Negroes," whereas Phelps[31] has expressed the belief that "the rates are about equal in the two races." Unfortunately, neither of these clinical impressions is supported by precise statistical data.

Phelps[4] has made the statement that cerebral palsy is equally prevalent among "children born in an outstanding city obstetrical hospital and the children born in the mountains of Maryland and West Virginia, where the children are usually delivered either by a grandmother or nobody." Again no statistical details were given to support this impression. The possibility that children born with brain damage have less chance of survival and of a consequent diagnosis of cerebral palsy in the mountains of Maryland and West Virginia than in the hospital was not mentioned. If one could assume that Phelps's figures showed equal prevalence rates in different regions of the United States, one would also have to know whether the proportion of obstetric complications was the same in the hospital and in the rural home deliveries. Since women who have complicated deliveries are generally sent to the hospital, a bias is probably introduced into the comparison. Phelps's general conclusions would suggest that so-called good obstetric care would not necessarily influence the cerebral palsy prevalence rate, and that the rate of cerebral palsy in the population is an inherent factor presumably not to be altered by improved obstetric practices. This conclusion would seem unwarranted on the basis of the facts—or, more correctly, in the absence of the facts—and again emphasizes the need for "the sense of caution required for the numbers [statistics] game."[32]

TABLE 2
ESTIMATES OF FREQUENCY OF CEREBRAL PALSY (EUROPE)*

	Number affected per 100,000 population				
Country	All ages	5 to 9 years	5 to 15 years	20 years or less	Number per 1,000 births
Norway (Ostfold County)	147†	234	—	147	1.9
Denmark	135	208	—	—	1.6
Sweden	65 to 130	—	—	—	0.6 to 1.2
Scotland	—	—	120	—	—
Scotland, Edinburgh	—	—	—	—	2.3
England (Birmingham and neighboring counties)	—	—	90	—	1.0

*For sources of data, see appendix A.

†Assuming a normal life expectancy after age five years.

ROCHESTER, MINNESOTA SURVEY

Method. In this survey all cases of central nervous system disorders diagnosed and coded in the Mayo Clinic records for the 30,000 residents of the community of Rochester, Minnesota during the period 1945 through 1954 were included. More than 30 diagnostic categories of the Mayo Clinic record system were reviewed, including the following diagnoses: Little's disease, cortical paralysis, cerebral infantile or birth or childhood paralysis or palsy, cerebral paraplegia or paraparesis, diplegia or hemiplegia, idiocy, tremor, chorea, athetosis, extrapyramidal disease or syndrome, and so forth. Those cases which fit the definition of cerebral palsy described above are included here.§

A separate analysis was made for many neurologic categories. Among these, there were 74 cases in which an abnormality of cerebral motor function presumably developed before the neonatal period and was first noted during infancy. Table 3 reveals that, for the entire period, about one-third of the cases (27 of the 74) were classified as cerebral palsy, whereas about two-thirds (21 of 34) of these patients who were surviving on "prevalence day" at the end of the study period were classified as having cerebral palsy.

The statistical results to be presented here for cerebral palsy are recognized as minimal values for the community, since mild cases in particularly may be underrepresented in this material.

Detailed reviews of clinical and etiologic classification of cases are available in other reports.[10,13,14,33] In view of the limitations incorporated in the definition of cerebral palsy in this study (and expected to be used in other studies utilizing various sources of medical records elsewhere), a simple classification of cases on the basis of principal clinical characteristics similar to that of Courville[11] was adopted here.

Results. The cases of cerebral palsy were divided into those which were predominantly monoplegic or hemiplegic; those in which spasticity, particularly of both lower extremities (spastic diplegia), was prominent; those referred to often as the "ganglionic syndrome," in which symptoms referable to the basal ganglia may be noted; and those in which ataxia was prominent. In the ganglionic syndrome group, hyperkinetic manifestations, such as chorea, tremor, athetosis, or dystonic movements, are present, usually combined with some spastic weakness. In the group in which the kinetic disability occurs in the form of ataxia, in combination either with spasticity or with flaccid weakness, involvement of the cerebellar system is believed to be present.

The 27 cases were classified as follows: 12 hemiplegic, four monoplegic, eight "spastic," one ganglionic syndrome, and two of the ataxic type. In most cases, involvement was probably more widespread than the heading of the classification group would suggest.

During the period of study, only three of the hemiplegic and six of the "spastic" patients

§The medical facilities of Rochester, Minnesota, are to a large extent concentrated within the organiation of the Mayo Clinic. About 98 per cent of the community births occur at St. Mary's Hospital and all newborn infants there are examined by members of the section of pediatrics of the clinic. Almost half of the resident population of the city are examined each year by Mayo Clinic physicians at the clinic or one of the local hospitals or at home for emergency house calls. The records for any of these examinations are incorporated in the clinic files, and the diagnosis made by each consultant during the patient's period of registry is cross-indexed by means of a system using IBM punch cards and tabulating devices. It is a relatively simple task to obtain the records of all patients who are residents of the city for practically any clinical disorder.

At the time of this study there were only a few physicians in general practice in the community and these referred practically all patients with serious or persistent neurologic or orthopedic impairment to the large staff of specialists at the clinic.

TABLE 3

CASES OF DIAGNOSED BRAIN DISEASE* AFFECTING THE MOTOR SYSTEM IN INFANTS AMONG THE RESIDENT POPULATION OF ROCHESTER, MINNESOTA, 1945 TO 1954, INCLUSIVE

Diagnosis	*Total, 1945 to 1954*	*Residents having specified disease alive December 31, 1954*
Hydrocephalus (infants)	24	6
Mongolism	19	5
Encephalodysplasia	1	0
Werdnig-Hoffmann paralysis	1	1
Tay-Sachs disease	1	0
Epiloia	1	1
Subtotal	47	13
Cerebral palsy†	27	21
Total	74	34

*Excluding recognized encephalitis and trauma after the neonatal period and one case of retinoblastoma extending to the cerebrum.

†For definition, see text.

were born in Rochester; the birth rate for the two groups combined is 0.6 per 1,000 births. As explained previously, this should be considered as a minimal estimate.

On prevalence day, 21 of the patients were known to be living in Rochester. The prevalence rate is thus about 0.7 case per 1,000 total population, or 1.6 cases per 1,000 population less than 20 years of age. The age distribution of the patients living in Rochester on prevalence day was as follows: 0–9 years, seven; 10–19 years, seven; 20–29 years, three; 30 years or more, four. (A more detailed analysis by clinical type was carried out and is included in appendix B.)

This rate is appreciably lower than that reported in other United States surveys and is similar to that reported for the Scandinavian countries. No etiologic significance can be attached to this fact, since, in the surveys in New York and Connecticut, case finding was probably fairly good but the definition of cerebral palsy was very broad. In the Scandinavian surveys, on the other hand, the definition stated or implied was more specific but case finding was less intense.

COMMENT

The statistical surveys of cerebral palsy reviewed here represent an expensive and time-consuming effort at collecting data on groups of cases of illnesses which, for the most part, are not comparable. If one is interested only in an approximation of the prevalence of cerebral palsy for medical care and planning purposes, the estimate of Altman[3] of about three to three and a half cases per 1,000 population would seem helpful. To the epidemiologist, however, the value of the statistics is in their disclosure of similarities or differences in frequency in populations or in segments of a population which may direct more definitive clinical or laboratory research concerning etiologic mechanisms. As emphasized in earlier paragraphs, the methodologic differences and the vagueness of the definition of cerebral palsy in the surveys reviewed prevent any sound statistical comparisons.

There was an appreciable discrepancy between the rates obtained in the Rochester, Minnesota population and those obtained in most of the other surveys in the United States. In the former study, there were about two cases of cerebral motor dysfunction with a specific diagnosis for each case accepted as cerebral palsy. In many of the other surveys, all such cases of cerebral motor dysfunction would have been classed together as cerebral palsy.

A retrospective attempt to determine the possible causal relationships of various prenatal and natal factors for the small number of cerebral palsy cases in the Rochester, Minnesota survey was not carried out at this time.

The highest rates for cerebral palsy reported were those from Schenectady County, New York. However, the incidence rates in other counties of upstate New York are said to be appreciably lower than in Schenectady County, and there is some question whether the estimates obtained in the Schenectady County study were excessive.[34]

In several surveys it seems that the investigators have been swayed by the enthusiasm of lay cerebral palsy associations into endowing their patient populations with normal life expectancy. Examples of this have been cited where the prevalence in the total population is estimated on the basis of prevalence rates in younger age groups and a normal or near normal life expectancy. The relative absence of cerebral palsy cases in older populations may in part be due to methods of case collection in the surveys, but some, and perhaps most, of it may also have been due to early death of the patients in previous decades. Improved medical care today means that a higher proportion of brain-injured infants will survive as cerebral palsied children. The same influence of improved medical care will lengthen life, but it is doubtful that life expectancy of the cerebral palsied will be increased to normal.

In most of the surveys a retrospective study of the medical history of parents (so-called cross-sectional study) was obtained to elicit possible etiologic mechanisms of cerebral palsy. The absence of normal controls in such comparisons has already been commented on.

In addition to the retrospective study of cerebral palsy patients, there has recently been a concerted effort to study systematically perinatal deaths and cerebral palsy cases in which necropsy has been performed.[35]

Studied retrospectively, each of these groups (perinatal deaths, living patients, and necropsied cases) provides only a partial and perhaps distorted picture of the nature and causes of cerebral palsy because of the bias of collection of the material which comprises it. All three combined may provide a more complete picture than has been heretofore available, but only in the light of the normal "control" from which these cases arise can we hope to eliminate the distortion.

Retrospective studies have their sources of bias, but the "longitudinal" retrospective study (that is, one in which data recorded in the past are correlated with observations on individuals in the present) is subject to less bias, particularly memory defect or the tendency of parents of affected children to fix blame or to recall some items more clearly than the parents of normal children. One well-designed project of the "longitudinal" retrospective type was that reported by Lilienfeld and Parkhurst.[16] They studied the association of the development of cerebral palsy with various factors of pregnancy and parturition recorded in birth certificates. These data were compared for three groups—one with "cerebral palsy" (unfortunately not further defined), a second for stillbirths and neonatal deaths, and a third composed of all other births in the population from which these cases were derived. The association of prematurity, various obstetric complications, and operative procedures was noted for both the cerebral palsy cases and the neonatal deaths.

These authors[16] and more recently Pasamanick and associates[18] and Knobloch and associates[17] have made reference to a "continuum of reproductive casualty" and have stated that certain abnormalities of childbearing in addition to prematurity, such as toxemia, bleeding during pregnancy, malpresentations, and so forth may frequently be associated with the lethal and sublethal members of this continuum. They include some forms of epilepsy, mental deficiency, childhood behavior disorders, and cerebral palsy as sublethal members of this continuum and the perinatal deaths (abortions, stillbirths, and neonatal deaths) in the lethal group.

Knobloch and associates[17] have recently reported on an anterospective study of the neurologic and intellectual sequelae of prematurity. They selected a group of premature infants and a matched group of full-term infants as controls and, after examining both groups over a period of several years, concluded that prematurity is directly correlated with cerebral palsy (unfortunately not further defined) and mental retardation. They suggested that such anterospective follow-up of individuals subjected to various abnormalities of childbearing may reveal a high incidence of several or all diseases associated with this "continuum of reproductive casualty" as compared to individuals not subjected to such potential stresses.

In the Rochester, Minnesota study a definition of cerebral palsy was adopted in which all disorders developing after the neonatal period, progressive neurologic disorders, and other well-recognized clinical syndromes and disease entities were eliminated.

The cerebral palsy category by this definition will include those patients with onset recognized prior to age two years in whom brain damage causing motor dysfunction was presumably present before the end of the neonatal period. Included in this still heterogeneous category are cases due to a variety of genetic, developmental, traumatic, and infectious factors. Subdivision of the cases by principal clinical characteristics has been recommended, since this seems to provide a reasonably sound beginning for further search for specific etiologic factors through clinicopathologic correlations as well as epidemiologic studies.

The "survey" reports by Phelps have been referred to on several occasions. These surveys were not systematic studies and his results which described the similarity of frequency from place to place are best considered as clinical impressions. Furthermore, the broad definition of cerebral palsy which Phelps has employed does not facilitate comparative statistical studies.

In referring to Little's description, almost a century ago, of a patient who had scissorlike gait, mental retardation, and speech difficulties, Phelps[4] stated that "the next 50 years saw nothing whatsoever done about these children . . . it became obvious that what was called Little's disease was only a particular subdivision of cerebral palsy. The name is fortunately relegated to medieval history, since it is quite clear the term Little's disease comprises but a small percentage of all cases of cerebral palsy."

It would seem that a retrospective statistical survey of Little's disease, a reasonably clear symptom complex as described above, would have provided far better prospects for clarifying the etiologic mechanisms involved in that disorder than the surveys to date have been able to provide for the numerous constituents of the cerebral palsy category as defined by Phelps or Perlstein. It would seem that what should be relegated to medieval medical history, so far as epidemiologic and perhaps other research is concerned, is the all-inclusive definition of cerebral palsy in common use today.

Perhaps an analogy of the present state of cerebral palsy research with the history of the development of knowledge about infectious diseases might illustrate one of the basic points

of this paper. Prior to Syndenham and others of his era who differentiated numerous infectious diseases, there was confusion regarding the natural history of the exanthemas, that is, the syndrome of rash and fever. Observers differed in their opinions of age distribution, severity, death ratio, seasonal incidence, sequelae, mode of transmission, type of causative agent, and other factors. The syndrome of rash and fever, as we now know, included a number of disease entities, such as rubella, rubeola, variola, varicella, scarlatina, meningococcemia, and so forth; and epidemics of these disorders alone or in combination naturally produced differences of opinion in regard to the clinical and epidemiologic characteristics of "exanthema." The differentiation of the specific disease entities through clinical and epidemiologic research has led to a clarification of their natural history and has provided the bases for prevention and control of most of the constituents of the rash-and-fever group today.

Somewhere between "Little's disease" and the bulk of neurologic disorders, as proposed by Phelps and others, lie the limits of a sound concept of the disorders which might best be grouped as "cerebral palsy." This group of disorders of unknown or uncertain origin which arise during the period of early brain development should be amenable to clinicopathologic correlation studies and epidemiologic research. Such research, it is hoped, will eventually eliminate this miscellaneous category of cerebral palsy by defining the nature of each of its constituents. Perhaps the definition proposed earlier in this paper and employed in the Rochester, Minnesota study is a step in the proper direction.

Such a specific definition may pose problems for lay groups and some clinical investigators. In this regard, it seems appropriate to present a statement made by Kennedy[36] in 1923 when the field of convulsive disorders was faced with many of the same problems discussed here for cerebral palsy. "To define explicitly may be futile or impossible; to describe, to classify, and to set boundary marks can be done with difficulty, maybe, but always with advantage to clarity of ideas. The effort to define may fail in its ultimate truth, but will show us often the scope of our endeavor and the nature of our objective."

SUMMARY AND CONCLUSIONS

1. The need for a precise definition of cerebral palsy in the enumeration of "cases" in a population is emphasized.

2. Most surveys reviewed here have been of the "cross-sectional" retrospective variety. In these studies cases in specified (and at times, unspecified) populations are collected and rates are developed and compared with the results in other areas. In addition to comparisons for geographic, racial, and economic conditions, detailed analyses of various suspected prenatal, natal, and postnatal complications have been made. Unfortunately, the incidence and prevalence rates obtained in these surveys are of little or no value for comparison, because cerebral palsy was either not defined or defined so loosely that only the investigator knew what was included or excluded as a "case." Furthermore, there was no uniformity of procedure in these surveys.

3. The survey methods employed by various investigators in the United States and Europe are reviewed. In these studies the definition of cerebral palsy stated or implied as a basis for case collections is as follows: "A group of conditions which affect the control of the voluntary motor system and have their origin in lesions of various parts of the brain." However, it is obvious that some undefined or poorly defined limits on age of onset and clinical type of abnormality not specified in the definition are employed in these studies.

4. In some of the retrospective studies described, there appeared to be some association of various childbearing complications with the presence of cerebral motor dysfunction; unfortunately, data of similar type for a comparable "normal" population were not available and the cause-and-effect relationship was left in doubt.

5. In a longitudinal retrospective study which was reviewed, data for patients and a large "normal" population born during the same period showed that prematurity and various obstetric complications and operative procedures were associated with cerebral palsy and neonatal deaths. Unfortunately, cerebral palsy was not defined in that study.

6. In anterospective research, one might begin with populations of conceptions or, more realistically, with newborn infants who could be subdivided into cerebrally "normal" and "abnormal" groups during a period of several years' follow-up. Perinatal deaths due to brain injury, as well as living patients with varying degrees of disability, would constitute the "abnormals." Recorded details of prenatal and obstetric history could be correlated with clinical and pathologic information for both the "normal" and the "abnormal" groups. Comparisons

for such groups might delineate significant exogenous factors, as well as genetic and other endogenous factors which might be related to the various categories of dysfunction.

7. Other authors have referred to the various lethal and sublethal abnormalities as a "continuum of reproductive casualty." These authors have recommended that complications of pregnancy and delivery which, on the basis of retrospective studies, are suspected of causing infant morbidity and mortality be studied specifically by anterospective and controlled technics. Such a study recently reported by these authors has helped to substantiate the impression that children born prematurely are more likely to have cerebral motor dysfunction and mental retardation than children born at term.

8. In a survey conducted in Rochester, Minnesota through the facilities of the Mayo Clinic, the prevalence of cerebral palsy was found to be less than that reported in most of the preceding surveys. This may have been due, in part, to differences in method of case collection, but the principal reason for the discrepancy relates to the viewpoint of what should constitute "cerebral palsy" cases in retrospective field research. In the Rochester, Minnesota study the following definition of "cerebral palsy" was adopted: Those disorders of unknown etiology arising during the perinatal period (from conception to the end of the neonatal period) in which motor dysfunction due to brain damage is recognized prior to the end of infancy. Disease entities of a progressive nature, such as epiloia or Tay-Sachs cerebral-macular degeneration, or well-recognized symptom complexes affecting motor function, such as hydrocephalus, mongolism, or encephalodysplasia, are not included in this cerebral palsy category. The constituents of the cerebral palsy group still form a heterogeneous combination and the diagnosis essentially becomes one of exclusion.

9. It is believed that the analysis of other disease entities and syndromes separately will result in a better-defined but still heterogeneous group of disorders known as "cerebral palsy" which are amenable to improved clinicopathologic correlations and epidemiologic research. Ultimately, it is hoped, such research will entirely eliminate the cerebral palsy diagnosis by defining the nature of its constituents and lead to prevention and control of the numerous disease entities included in the cerebral palsy category.

APPENDIX A

DETAILS OF SURVEYS OF CEREBRAL PALSY FREQUENCY IN VARIOUS AREAS OTHER THAN ROCHESTER, MINNESOTA

The studies by Phelps for various undefined areas in the United States have been discussed in the body of the paper. Other surveys will be considered here.

Schenectady County, New York Survey.[26] In Schenectady County information regarding all cerebral palsy cases known to any agency were obtained. Eighty per cent of 214 physicians in the county replied to a questionnaire regarding patients whom they had observed during the preceding five years. Hospital records for five years were reviewed, and various nursing homes and clinics supplied a list of the patients on their rosters. After duplications, deaths, and those who could not be identified were accounted for, 125 cases were registered. "In 67 cases, the diagnosis was checked by examination and evaluation by the orthopedic consultant." There is no statement regarding the accuracy of the diagnosis among the patients examined. The 125 cases are equivalent to a prevalence rate of 90 per 100,000 population for the total population. For the population less than 20 years of age, in which there were 85 cases, the prevalence rate would be 223 per 100,000 population (table 1).

In addition, a house to house canvass for cases in a sample population of 22,528 persons, comprising one-sixth of the estimated total population of the county, was carried out. In addition to the 20 known cases in this sample population, 14 cases not previously listed are reported. On the assumption that the sample was representative of the total county, it was estimated that the total number of cases was $125 + 6 \times 14$, or 209 cases.* This group of 209 cases in the county gives a prevalence rate of 152 per 100,000 for the total population, or for the population less than 20 years of age, 381 per 100,000 population.

The highest age-specific rate was found in the group five to nine years inclusive, where it was estimated to be 634 per 100,000 population or, for the "congenital cerebral palsy" cases, 591 per 100,000 population. The high rate in this early school age group rather than in the preschool group is understandable, since school age children are more likely to be observed for physical defects and since motor dysfunction is more difficult to

*This, too, must be considered a minimal figure of cerebral palsy as defined in this study, since, according to Wishik,[27] house to house canvasses miss 8 per cent of cases known to medical sources; and medical sources alone, according to Trussell and associates,[27] fail to report at least 25 per cent of cases which in most chronic disease surveys can be located by house to house canvasses.

recognize in infants and young children than in school age children. The children more than ten years of age with milder disease who do survive may make some adjustments which enable them to do without the continuous social and medical follow-ups which serve as important case finding sources in such surveys.

From this figure for congenital cerebral palsy, Fraenkel and associates[26] calculated a birth incidence of approximately six cases of cerebral palsy per 1,000 births† for Schenectady County.

Connecticut survey.[5] In Connecticut a study of cerebral palsy in the population of the state was made. Most hospital and social agency records were reviewed for only one year; other hospital records were reviewed for five or ten years. Inquiries to physicians apparently set no limit on the date in the past when the patient may have been seen. Seventy-six per cent of the 2,900 physicians queried replied. No house to house canvass was made, but the "correction factor" of the Schenectady County survey of 14 undiscovered cases per 20 reported cases was used to obtain the "true" prevalence rate for each county and for the state.

The cases of 1,519 affected children less than age 21 years were located. In a sample of 185 of these followed, about one-third were found to have moved, to have died, or to have a diagnosis other than cerebral palsy in the opinion of the orthopedic consultant.

On the assumption that this sample was representative of the total, the rate for incidence 20 years or less was estimated to be approximately 170 per 100,000 population. If the "correction factor" of the Schenectady County experience was applied, the "true" prevalence rate of approximately 288 per 100,000 population 20 years of age or less was obtained. This is still somewhat less than that reported in Schenectady County but, since the methods differed in the two studies, no conclusions can be drawn about the differences observed.

Clarke and Oconee Counties, Georgia.[27] In two counties in Georgia with a population of 54,291, a publicity campaign to locate all handicapped children was carried out by local and state health officials. Patients reported as having neurologic disorders were examined by a medical team which included a neurologist. A house to house canvass of a sample of the population totaling 4,840 persons was carried out; 1,373 members of the sample were 20 years of age or less. On the basis of the limited data available, the prevalence of cerebral palsy in persons 20 years or less in this population was estimated at five cases per 1,000 population.

Minneapolis, Minnesota.[19] Pohl reported as follows: "Statistics from the city of Minneapolis, Minnesota indicate that a child with cerebral palsy is born and survives on the average once for each 568 live births."

Baltimore, Maryland.[20] Anderson was aware of 33 cases of cerebral palsy among 11,196 live births at the Johns Hopkins Hospital for the period 1945 to 1949, inclusive. This gave a birth incidence of 2.9 per 1,000 live births, admittedly a minimal figure.

Birmingham and Neighboring Counties, England[6] *and Edinburgh, Scotland.*[21] The reports of the survey by Asher and Schonell in Birmingham and by Ingram in Edinburgh are based on incomplete returns and examinations of suspects reported from a variety of sources of medical information in these areas. The survey period for Birmingham is not stated; that for Edinburgh was for children born from 1938 to 1952, inclusive. In Birmingham about 70 per cent of the physicians replied to a postal inquiry about their cases; in Edinburgh general practitioners were not systematically queried and most case reports were obtained from an extensive review of educational, welfare, and medical institutional records and query of personnel in such institutions.

In Birmingham the prevalence of cerebral palsy in the population aged five to 15 years was estimated as 90 per 100,000. This is considerably less than that reported in the preceding surveys. The authors consider that this is a minimal rate for the area but point out that "results are similar to those of Professor Mackintosh who, in an address to the British Council for the Welfare of Spastics (1936), estimated that there were 1.2 cases of cerebral palsy per 1,000 children of school age in Scotland."[6]

In Edinburgh the number of cases of cerebral palsy for the preceding 15 years was estimated as 2.3 per 1,000 births.

Sweden.[25] Nilsonne reported that a survey made with Jonsätter and Haage of school age children in Sweden through school physicians, pediatric and orthopedic sections of hospitals, and institutions for cripples and mentally retarded provided 471 cases in 1944-1945. Physicians in private practice were not queried and no house to house canvass for cases was made. From the data obtained, Nilsonne estimated that one to two new cases per 100,000 population developed each year in Sweden. With a birth rate of 16.5 births per 1,000 population, the birth incidence would be 0.6 to 1.2 per 1,000 live births. Andersen's[7] estimate of prevalence as 65 per 100,000 population is based on the rate of one new case per 100,000 population, if one assumes an average duration of 65 years of the affected. Since Nilsonne set his rate as between 1 and 2, the range of prevalence rates would be 65 to 130 per 100,000 population on this basis (table 2).

Birth Incidence in Denmark.[23] Thomsen developed a case register from inquiries to practicing physicians and various hospitals in different cities in Denmark for the age group less than 16 years.

†This is compared with Phelps's estimate of new patients born of six per 100,000 population which, at a birth rate of 15 per 1,000, would be four per 1,000 births and is said to be within sampling error of the findings in Schenectady County.

He examined the patients and estimated the minimal incidence in Denmark as about 1.6 per 1,000 births and the minimal prevalence rate for ages five to nine years as 208 per 100,000 population.

Prevalence in Norway.[7] Andersen collected cases of suspects of less than age 21 years from various medical and lay sources in Østfold County. He examined all suspects personally and accepted the diagnosis of cerebral palsy in 69 per cent of the cases reported from physicians and in about 44 per cent of the cases found by the lay canvassers. He regards his rates as minimal values for estimation of prevalence because of the likelihood that "a number of cases must certainly have escaped detection." Eighty-four patients less than 21 years of age were observed. The prevalence rate for this population less than 21 years of age is 147 per 100,000 population. Assuming that the average duration of life of these patients was 65 years, the rate of 147 per 100,000 is the same for the total population. The highest prevalence was found in the age group five to nine years, in which it was 234 per 100,000 population. From this, the birth incidence was estimated at 1.9 per 1,000 births.

Andersen classified his cases by clinical type according to the system of Phelps and compared his results with those from other sources. He noted a smaller percentage of quadriplegic children in his material and felt that this was due to his more complete survey method, which located a higher proportion of mild cases than others had reported. He also reviewed the prenatal and obstetric histories and found a higher proportion of children of younger mothers than in the normal population and a higher proportion of the firstborn among the patients than in the normal population.

APPENDIX B

DETAILED ANALYSIS BY CLINICAL TYPE OF CEREBRAL PALSY CASES IN RESIDENT POPULATION OF ROCHESTER, MINNESOTA, 1945 THROUGH 1954

1. *Hemiplegic and Monoplegic Types.* There were 12 patients (five male, seven female) with hemiplegia (five left, seven right) and four patients (two male, two female) with monoplegia (two right lower, two left lower). Of these 16 patients, eight had been born in Rochester, six of these prior to 1945. Of the eight born elsewhere, five were born prior to 1945. In eight of the cases, the first Mayo Clinic diagnosis was made after 1944; in the remaining eight, it was made prior to 1945. On prevalence day, 14 patients (six male, eight female) were living in Rochester, one child had died elsewhere at the age of three years, and the other was apparently living elsewhere. Ages of the 14 resident patients were as follows: 0–4 years, one; 5–9 years, two; 10–19 years, four; 20–29 years, three; 30–39 years, two; 40 years or more, two.

Of the 12 patients with hemiplegia, six also had convulsive episodes, usually of a focal nature, but often progressing to generalized convulsions. Four of the 12 were also considered to be mentally retarded, and three of the 12 had strabismus associated with extraocular muscle palsy.

Of the four patients with monoplegia, none had convulsions or strabismus and none was considered mentally retarded.

2. *"Spastic" Type.* There were eight patients (all male) in whom cerebral palsy with spasticity, particularly of the lower extremities, was the prominent clinical picture. Two of the patients were premature at birth, and the mother of one had eclamptic convulsions at the time of delivery. One other full-term birth occurred during a convulsive period of the mother, which was said to be due to hypertension. The delivery of the other five children was reported as uncomplicated.

All eight were born in Rochester, five after 1944. In six of the eight cases, the first Mayo Clinic diagnosis was made after 1944. One child died during the study period, at age four years and, at necropsy, cerebral atrophy was noted; six of the seven survivors were residents within the city limits on prevalence day.

Six of the eight also had convulsive episodes, five were considered mentally retarded and four had strabismus due to extraocular muscle palsy. Speech impairment was reported in half the cases, and in one patient there was slight ataxia as well as spasticity.

On prevalence day, the age distribution of the six resident patients was as follows: 0–4 years, three; 5–9 years, one; 10–19 years, two.

3. *Hyperkinetic Manifestations.* These were infrequently described. One patient is classified in the ganglionic syndrome group. He was born in 1950. At birth spontaneous respiration did not occur for many minutes, and this was believed to be due in part to a difficult delivery in which the cord was wound tightly around the neck. Signs of decerebrate rigidity and later some hyperkinetic movements were noted. He had convulsive disorders, was blind, deaf, and retarded. He survived to age 18 months, and, at necropsy, severe degeneration of the basal ganglia and the white matter was noted.

4. *Ataxic Type.* In two other patients, both female, there was evidence of poor coordination from infancy. Both were born elsewhere prior to 1945 and moved to Rochester during the study period. One patient, aged 11 years and living in Rochester on prevalence day, had slight ataxia and coarse nystagmus with only minimal spasticity of the extremities. She was mentally retarded. The other patient had unsteady gait and slight athetoid movements of the upper extremities. She was 20 years old when examined at the Mayo Clinic. There was only minimal spasticity. She had moved out of Rochester prior to prevalence day.

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■ The researches of Mr. Lockhart Clarke prove very clearly that the filaments, comparatively few in number, which go from the posterior roots of the spinal nerves to the posterior columns of the cord, do not end in those columns, but pass through them to the part to which the other and more numerous filaments composing the roots pass directly—that is, to the central gray matter of the cord; and thus it is not difficult to see why the posterior columns can be cut across without benumbing the parts behind the section—why a result should follow which would not be possible if those columns were the continuation of the posterior roots of the spinal cord.

C. B. Radcliffe in *On Diseases of the Spine and of the Nerves*, published in 1871.

A Clinical Test for Sound Localization and Its Applications

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THE TEMPORAL LOBE is known to have an important auditory function, but no cerebral dominance for audition is established similar to that for speech, vision, and somatic sensation.

Audiometric studies following temporal lobectomy and in cases of unilateral temporal lobe lesions are not consistent enough to be of lateralizing value. We have been impressed by the fact that a more consistent defect following a temporal lobectomy is the failure to accurately localize the source of sound in the opposite auditory field by using a simple bedside tuning fork method. Even with this simple test, it is clear that this impairment is frequent and warrants further consideration.

This project was started with the idea of designing a simple, readily performed, accurate clinical test for sound localization. Once the test was standardized, a quantitative normal range was established and the defects in a preliminary group of cases were observed.

The journals devoted to clinical neurology contain few papers concerning the problems in relation to sound localization, so that a review of the accumulated data is indicated. The world literature is very extensive and diversified, for which reason an attempt is made to group the studies into two categories. One group is concerned with the role of sound physics and peripheral factors in sound localization, and the other deals with the role of the central neural mechanisms.

According to Boring,[1] the psychologists of the nineteenth century, for the most part, doubted the existence of any real auditory space perception. The empiricists, like Berkeley, Mill, and Bain, accepted the hypothesis that past experience was the basis for sound localization.

The modern concept of auditory space perception began, perhaps, with the observations of the Webers. E. H. Weber[2] made the observation that, when two watches were placed near an observer's ears, they could both be heard simultaneously and each could be referred to its proper side. This perhaps marked the origin of the idea that the primary dimension of auditory localization is left and right. E. F. Weber[3] studied sound localization with the observer's head submerged in water, and from his results concluded that sound could not be localized accurately except from left to right. He erroneously attributed sound localization to tactual differences at the external canal.

Bloch,[4,5] studying sound localization, found that the source of sound is better localized in front in the median plane, less accurately localized in the back, and least accurately from the sides. He also noted that there is no confusion of left and right. Matsumoto[6] in 1897, using a sound cage for the first time, duplicated Bloch's experiments.

In attempting to explain the mechanisms involved in sound localization, out of the variety of experiments and works three theories have been postulated: the intensity theory, the phase theory, and the time theory. The intensity theory, which is the oldest of the three, is based on the principle that when two sounds, varying only in intensity, are led to both ears simultaneously, the observer will tend to localize the sound toward the side where it is of greater intensity. The phase theory is based on the observation that when two tones, varying only in phase, are led to the ears of an observer, he will tend to localize the source of sound as coming from the side of the leading phase. The time theory is based on the principle that when two sharp sounds, like two clicks, varying only in time, are led to the ears of the observer, he will localize the sound as coming from the side of the first arrival. The only difference between the time and the phase theory is that the first depends on the time of arrival of a single sound, while the second depends upon the time of arrival of the crest of the wave phase of a sound, like a pure tone.

Many reports in the literature favor the intensity theory.[7–20] Lord Rayleigh[8–11] definitely established the theory and the fact that voices are localized easier than pure tones. Thompson[15–17] built his pseudophone with an attached artificial pinna, and his experiments favor the intensity theory. He also demonstrated the effect of the external ear in the localization of sound.

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Thompson[21] inaugurated the phase theory in 1878. Support to the theory came from the works of several authors.[8–11,22–25]

The time theory was first proposed by Mallock[26] in 1908 and was demonstrated experimentally by Aggazzotti[27,28] in 1911. Definite support to the time theory came from the work of von Hornbostel and Wertheimer[29] and later from Klemm.[30]

Halverson[31–33] studied both factors in localization and concluded that the phase difference was more effective than the binaural intensity ratio in accurate localization of sound.

In 1928 Young[34] demonstrated the phenomenon of left and right reversal of auditory localization with the use of the acoustical transposition of the ears by means of his reversal pseudophone.

The arguments between those in favor of the intensity theory and those in favor of the time or phase theory ended with the work of Trimble,[35,36] who brought all the observations together and attributed the localization of low tones to the phase difference and the localization of high tones to the intensity ratio.

Investigating the localization of pure tones, Stevens and Newman[37,38] discovered that the ability to localize tones varies markedly with variation of the frequency. From their findings it is established that localization is good until it reaches the 1,000 cycle tone, when it becomes increasingly worse between 2,000 and 4,000, but is accurate again at a high frequency, roughly about 6,000 cycles (figure 1). Their findings supported Trimble's view that localization of low tones is mainly by phase difference, while localization of high tones is by intensity ratio difference. They explained the reason why complex sound was localized better than a pure tone by the fact that the first contains a combination of both low frequencies and high frequencies.

Recent work in the localization of pure tones by Langmuir[39] in 1944 and Hirsch[40,41] in 1948 agrees in restricting the importance of interaural phase difference to frequencies below 2,000 cycles.

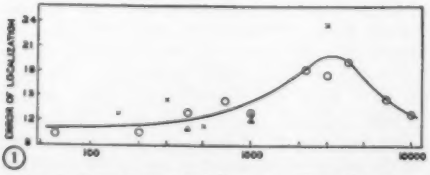

FIG. 1. From Stevens and Newman. The ordinate in the above figure represents the errors in degrees made by the subjects at different frequencies. Note that at 3,000 cycles there is a critical region in which localization is very poor.

The effect of sound stimulation upon an observer in a reverberant room has been the subject of study by Langmuir[39] and by Wallach, Newman, and Rosenzweig.[42] From the work of these investigators we have learned that some sounds fuse into a single auditory sensation if they are closely spaced in time. The mechanism for the localization of sound in a reverberant room is based on the fact that the first sound to arrive at the listener's ears tends to be the determining factor in localization of the source. Apparently, the fusion of the sounds and the arrival of the first sound seems to be the accepted explanation for the ability of observers to accurately localize sound stimuli in a highly reverberant room.

Jones and Bunting[43] studied the displacement after-effect in auditory localization. They found that the effect of the sustained stimulation is to displace the objective midpoint toward the direction of the sustained tone.

Laborde[44] suggested that the semicircular canals were the means by which sound was given spatial position. Preyer's[45] and later Munstterberg's[46] experiments were in favor of Laborde's theory. However, definite evidence against this theory came from the works of Breuer[47] and von Kries;[48] the latter revealed that the capacity of an observer to localize simultaneously both a noise and a whistle discarded Laborde's explanation, since the head could not move in two directions at once.

Clark and Graybiel[49] and Arnoult[50] studied the audiogyral illusion or postrotatory localization of sound. Graybiel and Niven[51] determined the effect upon the localization of sound in a subject placed in a centrifuge. When the subject is faced toward the center of the centrifuge, he tends to localize the source of sound as coming from below its actual source, but if faced away from the center of the centrifuge, he localizes the source of sound as coming from above its actual source.

Wallach[52] studied the role of head movements, vestibular, and visual cues in sound localization. The effect of position and eye movements on the localization of the sound source was investigated by Ryan and Schehr.[53]

The localization of the distance of the source of sound has been the subject of study by Klemm and Arps[54] and Wightman and Firestone.[55] From their studies it is apparent that the total intensity of the sound gives a clue that enables one to determine a certain but limited localization of its distance.

THE CENTRAL NERVOUS SYSTEM IN SOUND LOCALIZATION

Besides the peripheral factors already considered and in order to accurately localize the source of sound stimuli, we must be equipped with the brainstem pathways that convey impulses from the auditory nerves to the cortex. The afferent pathways for sound localization will follow, of course, the same pathways of hearing in general (figure 2).

Kemp, Copee, and Robinson,[56] studying the electrical responses of the brainstem of cats to bilateral auditory stimulation, found that responses from the homolateral and contralateral components in the lateral lemniscus were practically equal in threshold, latency, and amplitude. Ades[57] and Ades and Brookhard[58] also studied the auditory midbrain mechanism in cats. Among other things, it is reported that the trapezoid body is by far the most important site of crossing in the auditory projections and there is no connection between the two geniculate bodies via the commissure of Gudden. The contralateral ear has a greater contribution to the inferior collicular response than the homolateral ear. Rosenzweig[59] has demonstrated binaural interaction at the level of the inferior colliculi in cats. His studies suggest that interaction may occur at lower levels; however, more investigation is required before this problem is completely understood.

New possible afferent pathways from the cochela to the auditory cortex and efferent or recurrent pathways from the higher center to the cochlea have been reported.[60–65] However, it is beyond the scope of this paper to go into any detail discussion of these studies.

Since Ferrier's[66] original work on temporal lobe ablations in monkeys several other studies have been done in the same animal, as well as in baboons and dogs.[67–69] Ferrier's animals were described as deaf following bilateral temporal lobe ablation; however, other studies failed to support his findings. Other investigators reported no disturbances in audition nor in behavior, but stated that the animals localize the source of sound poorly. A state of psychic deafness similar to the syndrome of psychic blindness of Kluver and Bucy[70] was reported subsequent to bilateral temporal lobe ablations in dogs.[69] Culler and co-workers,[71,72] working on cats, reported that ablation of one auditory cortex produced a hearing loss of three to five decibels.

The role of the temporal cortex in sound localization has been the subject of several studies in the past.

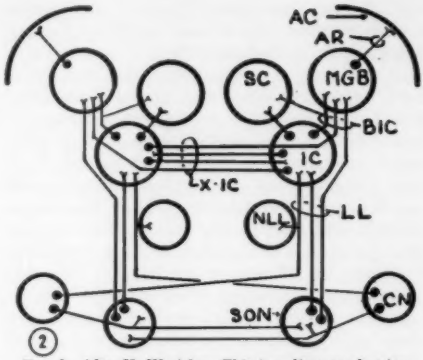

FIG. 2. After H. W. Ades. This is a diagram showing the established anatomic auditory pathways, with the addition of the new neurophysiologic connections. The neuron of the first order is situated in the spiral ganglion of Corti and sends its axon via the cochlear nerve to terminate in the cochlear nuclear complex. The second order neuron fibers either cross and ascend as a component of the contralateral lemniscus to terminate in the inferior colliculus, or they leave the cochlear nuclei to terminate both in the homolateral or contralateral superior olivary nuclei. The third order neuron fibers leave the superior olivary nuclei, ascend in the homolateral lemniscus, and terminate either in the inferior colliculus or the medial geniculate body. Other third order neuron axons leave the inferior colliculi via the inferior quadrigeminal brachium to terminate in the homolateral medial geniculate; still others leave the colliculus via the inferior quadrigeminal commissure to terminate in the opposite colliculus or pass through to join the brachium. The fourth order neuron fibers leave the medial geniculate body and project to the auditory cortex. AC—acoustic cortex, AR—auditory radiations, BIC—brachium of inferior colliculus, CN—cochlear nucleus, IC—inferior colliculus, LL—lateral lemniscus, SC—superior colliculus, SON—superior olivary nucleus, XIC—commissure of inferior colliculus.

From the works of Tanturi[73] and Rosenzweig[74] we learn about the electrical response of the auditory cortex of cats to individual stimulation of the ears by click sounds. Under conditions that will cause a sound to be heard at one side of the head, the cortical activity is greater at the contralateral hemisphere. When the sound is heard in the median plane, the cortical activity is equal at the two hemispheres.

The effect of bilateral auditory ablations upon the ability of rats and cats to localize sound in space have been reported.[75–80] The investigators agree that the operated animals show a marked impairment in their localizing function. This evidence is very suggestive of the important role of the temporal cortex in relation to sound localization.

Clinical observations in relation to the effect of temporal lobe ablation or lesions upon hearing and sound localizations in man began

with the observations of Ferrier. He quoted a case of Shaw and a case of Wernicke and Friedlander, in both of which complete deafness occurred; at autopsy extensive damage to both temporal lobes was found bilaterally. Frazier and Rowe[81] reported that, in temporal lobe tumors, when obvious deafness was present it was usually contralateral, and if auditory hallucinations were present they were usually contralateral to the side of the tumor. Penfield and Rasmussen,[82] by electric stimulation of the temporal cortex in man, were able to create the illusion of sound that the subjects on some occasions referred to the contralateral ear, Wortis and Pfeffer[83] reported a case of a right temporal parietal-occipital lesion with disorientation of sound localization on the left.

Bocca and co-workers,[84] studying patients with temporal lobe lesions, confirmed the observation that tonal audiometry is not of lateralizing value because of its inconsistent findings. He proposed the use of distorted voice audiometry as a much more useful test; however, in seven of his 18 cases the test failed to show a definite defect in proved temporal lobe lesions.

METHOD AND PROCEDURE

It was decided to determine first the performance of normal individuals in localization of the source of sound coming from a horizontal plane while they are blindfolded and unable to move their heads. In this way, visual, vestibular, and head movement cues are eliminated. Since it is known that a complex sound is better localized than pure tones, such a sound stimulus is provided. Using a Maico H I model audiometer, after turning the power control switch on, one proceeds to set the masking control at 90 decibels. Under this condition, when the output selector is turned to air mask, a complex sound is created which comes out through the red receiver. This sound consists of a fundamental frequency of 60 cycles per second. On listening to the tone, the 60 cycle predominates over the background sound, which is created by all the harmonic frequencies of the fundamental 60 cycle tone. The sound is low in frequency and rasping.

The subject sits on a stool, facing a Ferree-Rand type of perimeter with an arc of 330 mm. radius. The purpose of the test is explained to the subject. He is then blindfolded and his head immobilized by supporting the chin at the adjustable chin-rest of the perimeter. Care is taken to maintain accurate, equal distances from the ears to the edge of the perimeter. The subject holds in each hand a metal pointer 20 cm. in length and points toward the exact spot he thinks is the sound source. The sound is delivered from 13 different positions 15 degrees from each other on the left and right sides alternately. The receiver which is emitting the sound is moved from one position to the next, but it is always resting at right angles to the edge of the perimeter and with its anterior surface parallel always to the curve of the perimeter. Care must be exercised not to cause any extraneous noise which will give the observer cues to the localization of the sound. The sound stimulus is never prolonged beyond 10 seconds, and the subjects are asked to localize the source within this time. At no time is the subject permitted to move his head. The ideal set-up is to have an assistant turn the switch to produce the sound while the other observer is placing the source of sound along the perimeter (figure 3).

Using this method, two series of normal subjects were done. The subjects were selected after audiometry showed no hearing defects and central or nervous system disorders were absent by history and examination. One series of 10 subjects was called the "not-well centered series" and in this group the biauricular axis was 11 cm. behind the 180° axis of the perimeter and the vertex of the head was above, at, or below the level of the source of sound. The second series, called the "well-centered series," consisted of 10 subjects in whom the biauricular axis was 4.5 cm. behind the 180° axis of the perimeter and the vertex of the head was at the level of the sound source. This position was obtained by moving the adjustable chin-support forward. The findings are recorded in the usual visual (perimetric) field chart, but are referred to as the "left and right auditory fields." The distance in degrees between the center of the source of sound and the end of the pointer is the error, which is referred to as the "angular deflection." The results of the two normal series are recorded in table 1.

Five cases of unilateral temporal lobe lesions of different etiology were studied. In these cases there was no marked involvement of the sensorium and no evidence of proprioceptive or cerebellar disease. The case reports and the results of the study are summarized in table 2.

DISCUSSION

The ability of human subjects, as well as animals of lower species, to localize the source

of sound is well known. The observations derived from the ablations studies in rats and cats and from the obstacle avoidance experiments in bats[85] are all suggestive of this ability. The localization of the sound source is possible because of the assistance of several cues. It is quite obvious that, if the object emitting the sound is visualized, the localization is visual as well as aural. If the visual cue is eliminated, the ability to localize the sound source rests upon the information obtained by proprioceptive head movements and vestibular cues, as well as from the information derived from the time of arrival and the intensity ratio of the sound at each ear. Sound coming from behind is shadowed by the position of the pinna and this is used as another cue which assists in localization of sound sources whether they are in front or behind.[15–17]

If an attempt to localize the source of sound as to whether it is coming from above or below a horizontal plane, or if an attempt is made to localize sound coming from the median plane as to whether it is in front of or behind the head, the head movements and vestibular cues are required. The importance of head movements rests on the fact that the subject can change the binaural phase and intensity by moving his head.[52,53] As far as the localization of the distance of the source of sound is concerned, the total intensity of the sound gives a clue that enables one to determine a certain but limited localization of its distance. A very important requisite for distance localization is

FIG. 3. This figure illustrates the way this test is performed. The subject is blindfolded and facing the perimeter with the chin resting at the adjustable chin rest. The ears are equidistant from the edge of the perimeter. The subject is attempting to localize the source of sound on the left with the assistance of a metal pointer. Note that the receiver emitting the sound is resting at a right angle to the edge of the perimeter and its anterior surface is parallel to the curve of the perimeter. An assistant is turning the switch of the audiometer. (The H-1 model audiometer in this picture is included with the permission of the Maico Company.)

TABLE 1

NOT-WELL CENTERED SERIES			WELL-CENTERED SERIES		
Subjects	*Average angular deflection in degrees for a complete test*[1]	*Difference in degrees between the left and right auditory fields*[2]	*Subjects*	*Average angular deflection in degrees for a complete test*	*Difference in degrees between the left and right auditory fields*
1	6.7	2.8 L[3]	1	9.0	1.5 R
2	9.3	3.8 L	2	8.6	4.8 L
3	9.0	0.3 R[4]	3	8.6	2.6 R
4	6.5	3.8 L	4	5.1	2.0 R
5	7.8	0.9 R	5	5.5	0.3 L
6	7.3	1.3 L	6	4.2	2.3 R
7	8.3	1.9 L	7	11.2	0.5 L
8	10.7	3.2 L	8	4.2	0.9 L
9	7.1	3.4 L	9	7.3	3.8 R
10	8.3	1.4 L	10	8.0	2.6 R
	Average—7.2°	Average—3.2°		Average—7.1°	Average—1.3°

Total average for 2 series (complete test)—7.2°
Total average difference between left and right auditory fields—2.25°

[1]The average angular deflection in degrees for a complete test is obtained by adding the angular deflections of 13 stimulating positions and dividing the result by 13.
[2]The difference between the left and right auditory fields is obtained by subtracting the average angular deflection in the most accurate field from the average angular deflection in the less accurate field.
[3]The L following the number means that the localization was less accurate on the left auditory field.
[4]The R following the number means that the localization was less accurate on the right auditory field.

TABLE 2

History and Clinical Findings	*Average Complete Test*[1]	*Left Aud. Field*[2]	*Right Aud. Field*[3]	*Difference between Left and Right Fields*
A 37 year old white male who had a grand mal seizure followed by intense headache 3 days prior to his admission to the hospital. At the time of admission was critically ill and stuporous. A large right temporal lobe abscess was found at operation. After surgery, visual fields revealed a left homonomous hemianopsia. Audiometrics reveals impairment of hearing at the 6,000 cycle on the left.	29.0°	44.0°	17.5°	26.5°
A 13 year old white female with a history of grand mal seizures 2 years prior to admission. Pneumoencephalogram suggestive of space occupying lesion at the right frontotemporal area. At operation tumor not visualized; the inferior third of the posterior portion of the right temporal lobe was resected. Postoperative x-ray therapy aimed to the thalamus. Audiometrics normal.	12.4°	21.0°	5.3°	15.7°
A case of a 35 year old white male with malignant hypertension, admitted with a right hemiparesis and aphasia. Clinically the diagnosis of left middle cerebral artery occlusion was made; spinal fluid transaminase was significantly high. Visual fields normal. Audiometrics revealed hearing loss in the right for the 8,000 and 12,000 cycles only.[4]	21.8°	7.8°	21.0°	13.2°
A 61 year old white male with a history of having grand mal seizures 5 years before his admission to the hospital. A past history of central nervous system lues. Pneumoencephalogram revealed a huge dilation of the left posterior ventricle, the left temporal horn, and a porencephalic cyst at the temporo-occipital area. Visual fields reveal a right homonomous hemianopsia; audiometrics revealed bilateral, symmetrical impairment of hearing for high frequencies.	8.8°	7.1°	13.0°	5.9°
A 28 year old white male with a history of seizures for 16 years. Clinically the diagnosis of right temporal lobe epilepsy (psychomotor) was made. The patient was operated and the right temporal lobe tip including the amygdaloid nucleus was resected to a point 3 cm. posteriorly. Following surgery audiometrics and visual fields were normal.	15.0°	19.0°	13.8°	5.2°

[1]The figures under this heading represent the average angular deflection for 13 positions.
[2,3]The figures under these headings represent the average angular deflection for the corresponding field.
[4]This case performed the test with the left hand only. Unpublished statistical data of studies in normal subjects revealed that a normal test is performed with either hand alone without any significant difference in the performance. In the above cases the auditory fields were done following surgery in the three operated cases. Note that there is a marked impairment of auditory localization for a complete test in three of the cases. In all the cases the contralateral auditory fields are very abnormal, particularly in the first three. The first case with the extensive temporal lobe abscess confused left for right on two occasions with the displacement toward the right.

that the sound must be a familiar one.[54,55]

Normal subjects are very accurate in their localization of sound sources when coming from a horizontal plane. The average angle of deflection from the sound source under the conditions of our experiments is 7.2°. It is quite evident that normal subjects make no mistakes distinguishing left and right positions. This previously established principle is supported by the findings in the 20 subjects tested. Their performance in the left auditory field, as compared to the right field, reveals a statistical difference of only 2.25°.

Of five cases of unilateral temporal lobe lesions studied, one subject confused left and right positions, but only on the contralateral auditory field. . This evidence is in favor of Boring's[1] observations that the primary function of the localization of sound is that of determining left from right, and that localizations in a vertical plane or in front or behind are perhaps a secondary function.

Displacement of the biauricular axis behind the 180° axis of the perimeter, as well as variation of the level of the vertex of the head, fails to alter statistically the accuracy of the performance to any significant degree.

Slight variation in the length of the time of stimulation failed to alter the accuracy of the localizing response; however, we like to emphasize that in the present study ten seconds was the maximum time of stimulation in order to prevent the after effect displacement as shown by Jones and Bunting.[43]

Investigators in the past considered different factors as being responsible for the localization of sound in space. E. F. Weber thought that tactual differences at the external canals was the important mechanism in sound localization. Laborde attempted to explain this phenomenon as a function of the semicircular canals. The effect of the shape and position of the pinna were studied by Thompson. Extensive studies are known in connection with the important role of the properties of sound as a contributing factor in the localization of its source. All these external factors are not per se the mechanism for sound localization; however, they play a significant role in this function.

To explain the neurophysiologic mechanisms responsible for sound localization, several investigators have proposed hypothetical sites and functions.[86–90] There is no definite neurophysiologic confirmation of any of these hypotheses as yet.

The important function of the temporal cortex in the localization of sound sources has been the subject of several studies in the past. Jacobsen and Elder,[68] after bilateral temporal lobe ablations in baboons, reported that these animals were not deaf but localized the sources of sound poorly. Pennington,[75–77] working on rats, and Neff, Yela, Arnott and Diamond,[78–80] working on cats, after bilateral ablations of the auditory areas, reported marked impairment in the acquisition of a habit requiring the localization of sound in space. Unilateral ablations studies in the above animals fail to reveal any impairment in the ability of the animals to respond adequately in a discriminatory situation requiring the localization of the source of sound in space.

In the five cases studied in the present report, impairment of accurate sound localization occurred in the contralateral auditory field. These findings are in agreement with previous clinical observations and with the animal experiments of Rosenzweig.[74]

In two of the cases of the present report tonal audiometry was normal, and in one case there was bilateral symmetrical hearing loss for high frequencies. Visual fields studies in two cases were normal, which brings one to the consideration that the auditory fields could be affected by lesions that do not involve the visual radiations in the temporal lobe.

The difference between the observations on unilateral temporal lobe ablations in animals and the results in man is believed to be due to the fact that in the animal experiments the visual and head movement cues were not eliminated as in our control study.

It is our belief that we are dealing with a specific acquired biologic function which is altered by unilateral temporal lobe damage in man; the defect caused by such damage could be determined by performing a test in sound localization. The area in the temporal cortex concerned with localization of the sound source has not been defined as yet. This is a problem that deserves further consideration.

The test described is simple and does not require any equipment not now available in any general hospital or clinic. Impairment of the sensorium or evidence of proprioceptive or cerebellar disease are obvious limitations to this test. This is only a preliminary report and obviously a more extensive study including pathologic correlations of the findings is warranted.

SUMMARY

1. The literature on sound localization is reviewed.

2. The functional anatomy responsible for the neurologic mechanisms of sound localization is discussed.

3. A clinical test for sound localization is described.

4. Two normal series under different conditions are reported. The average angular deflection in the normal series is 7.2°. The average variation between left and right auditory fields is 2.5°. Variations between left and right of 5° or more are considered significant.

5. Five cases of temporal lobe lesions were studied, all of them with impairment of the localization ability in the contralateral auditory fields.

6. The role of the temporal lobe in sound localization and the possibilities of this test are discussed.

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CASE REPORT

Acute Infantile Hemiplegia Secondary ot Spontaneous Carotid Thrombosis

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IN RECENT YEARS there has been increasing interest in the recognition and pathogenesis of spontaneous thrombosis of the carotid vessels in adults. The possibility that this syndrome may also occur in infants or children has not received the same attention. We believe this case represents the first reported instance of spontaneous thrombosis of the internal carotid artery in an infant. The histologic findings suggest one of the possible etiologic mechanisms involved.

CASE REPORT

A 16 month old Negro male was admitted to the Syracuse City Hospital on July 3, 1956 at 11:15 p.m. He was apparently well until one week prior to admission when he had a "cold" and nonproductive cough which lasted for two days. On July 1, 1956 he became irritable and slightly anorexic. The following day the child stumbled on his right foot, cried for a short time, but then appeared normal. At 12:05 a.m. on July 3 his mother noted that the sole of his right foot was pale and that the right foot was cooler than the left. When he attempted to walk, it was apparent that he was dragging his right leg. A few hours later his mother noted that the left corner of his lip was "drawn up" when he cried. She also noted that he held his head tilted to the left. The child was then seen by a private physician who suggested hospitalization for further study.

The child was born with a pulsating mass on the medial surface of his right upper arm which had increased in size recently. From the age of nine months, the child had passed several worms which were described as about six inches long and pointed at both ends. Otherwise the past history and review of systems were noncontributory.

General physical examination showed temperature 98.6° F., pulse 80, respirations 24, and blood pressure 110/?. Both ear drums were perforated but there were no signs of acute inflammation. There was moderate anterior and posterior cervical adenopathy. These nodes were nontender, freely movable, and rather firm. There was dullness to percussion posteriorly on the right from the midlung field down. Breath sounds were decreased in intensity in this area. The left lung was negative. The right brachial artery was seen to be dilated and serpentine in its course from the axilla to about 2 or 3 cm. below its origin. The right axillary artery also appeared dilated. The right leg was cooler than the left from the knee down and neither the dorsalis pedis nor the posterior tibial was palpable. The carotid arteries were not palpated. Both femoral pulsations were palpable and equal and the left dorsalis pedis and posterior tibial were palpable. The remainder of the general physical examination was negative.

During neurologic examination the infant responded only to painful stimulation. He lay in bed with the left leg flexed at the knee and the hip rotated externally. The right leg was rotated externally. The right upper extremity manifested rigidity. The right lower extremity was flaccid and had almost no muscle power. Deep tendon reflexes were present bilaterally but were more active in the right arm and leg than in the left. The Babinski sign was positive on the right but negative on the left. Cremasteric reflexes and abdominal reflexes were absent on the right but active on the left. Kernig and Brudzinski signs were negative. Cranial nerves appeared normal, except that the right eye was never closed completely. Pupils were round, regular, equal, and reacted to light. There was no nystagmus and both retinas were normal. Within 36 hours after admission both pupils became dilated and fixed, the state of consciousness became further depressed, and the child died on the third hospital day.

Postmortem examination: The autopsy was performed at Syracuse City Hospital on July 6, 1956, three hours post mortem. Significant findings include the following: The aorta showed no evidence of aneurysm or atherosclerosis. The right external iliac artery measured 0.2 cm. in diameter; the left measured 0.4 cm. An aneurysm of the right axillary artery was removed and appeared to be 2 cm. in length and to contain thrombus. The artery distal to the aneurysm showed a dilatation 2 cm. in length. Dissection of the carotid arteries in the neck did not disclose thrombosis or vascular anomaly. The remainder of the vascular system appeared normal.

The small intestine from the level of the jejunum to the ileum contained a great many ascaris worms. There was no dilatation or ulceration of the intestine, however.

After fixation the brain weighed 1,100 gm. (normal 1,040 gm.). The cerebral hemispheres were

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asymmetric, the left being considerably larger than the right, with deviation of the cingulate gyrus from left to right. There was flattening of the gyri and decreased depth of sulci bilaterally, more marked on the left side. There was marked softening throughout the left middle and inferior frontal gyri, as well as the pre- and postcentral gyri and the superior and inferior parietal lobule, extending to the parieto-occipital fissure and into the superior, middle, and inferior temporal gyri. Examination of the base of the brain revealed that the arteries were normal in caliber and distribution, except for the presence of thrombus in the left internal carotid artery (figure 1). This thrombus extended beyond the bifurcation into the middle cerebral and anterior cerebral arteries for 3 to 5 mm. The thrombus was grayish-black in color, firm in consistency, and adherent to the intima. The cut sections of the cerebral hemispheres revealed that the left hemisphere had softening in the white matter primarily, extending from a point 1 cm. posterior to the frontal pole to a point overlying the rostral extremity of the occipital horn. Within the putamen and globus pallidus extending across the internal capsule was a cystic area which measured approximately 1 cm. from side to side, 0.5 cm. in anteroposterior dimension, and 0.3 to 0.5 cm. in vertical dimension. The walls of this cyst were irregular and grayish.

MICROSCOPIC DIAGNOSIS

Brain: Multiple sections throughout the regions of gross softening showed evidence of congestion, edema, and small perivascular hemorrhages. In addition, there was a diffuse ischemic cell change, together with micro- and macrocystic changes. There was no evidence of phagocytosis.

Right brachial artery: There was aneurysm formation with an organizing thrombus. The intima was thickened and fibrotic. The internal elastic membrane was not present. The thinned media showed lack of elastic and muscle tissue with fibrosis (figure 2A). There was marked calcium deposition in the thrombus, intima, and media and adventitia of the vessel wall (figure 2B). There was an increased number of small vessels clustered within the adventitia.

Right external iliac artery: There was fibrotic thickening of the intima and fragmentation of the internal elastic membrane.

Left internal carotid artery: In several sections, there were flecks of calcium in the adventitia, with degeneration of surrounding connective tissue in the immediate area (figure 2C). In figure 2D the vessel is shown to be occluded by a recent thrombus consisting of agglutinated strands of platelets and leukocytes, with masses of fibrin and red cells between. No inflammatory changes were evident in the vessel wall.

The remainder of the microscopic sections showed no pathologic changes. No ascaris larvae were identified in any sections.

FIG. 1. Left internal carotid artery with protruding thrombus.

DISCUSSION

A complete clinical and pathologic study of spontaneous nontraumatic thrombotic occlusion of the internal carotid artery in infancy has not been reported previously.

Cabieses and Saldias[1] reported a case of spontaneous occlusion of the left internal carotid artery in a nine year old boy. This boy presented with a right hemiplegia, and evidence for carotid occlusion was based on failure of filling in angiography and palpation of the exposed vessel. This patient recovered; therefore, no histologic studies and no commentary regarding pathogenesis were available. Gross[2] reported two cases of internal carotid occlusion, both due to embolization from a thrombosed patent ductus arteriosus. His review included previously reported cases of arterial occlusion due to emboli or thrombosis.

Generalized arterial calcification in infants has been reported by Prior and Bergstrom,[3] Stryker,[4] and Field.[5] Medial calcification and internal fibroblastic proliferation were common to all these reports. Stryker felt that coronary occlusion in infants was nearly always due to this type of arterial disease. In regard to the genesis of arteriosclerosis, Blumenthal, Lansing, and Gray[6] concluded from their studies that the basic age change in the major arteries of man is primarily calcification of the media and that the rate of calcium deposition is directly proportional to the intensity and rate of elastic changes. Field[5] showed that the primary site of calcium deposition appeared to be the intercellular substance of the media, suggesting that an injury of this substance is the cause of the calcification.

The case presented here is important as the first report with histologic confirmation of thrombosis of the internal carotid artery in an infant. This entity should be considered in the

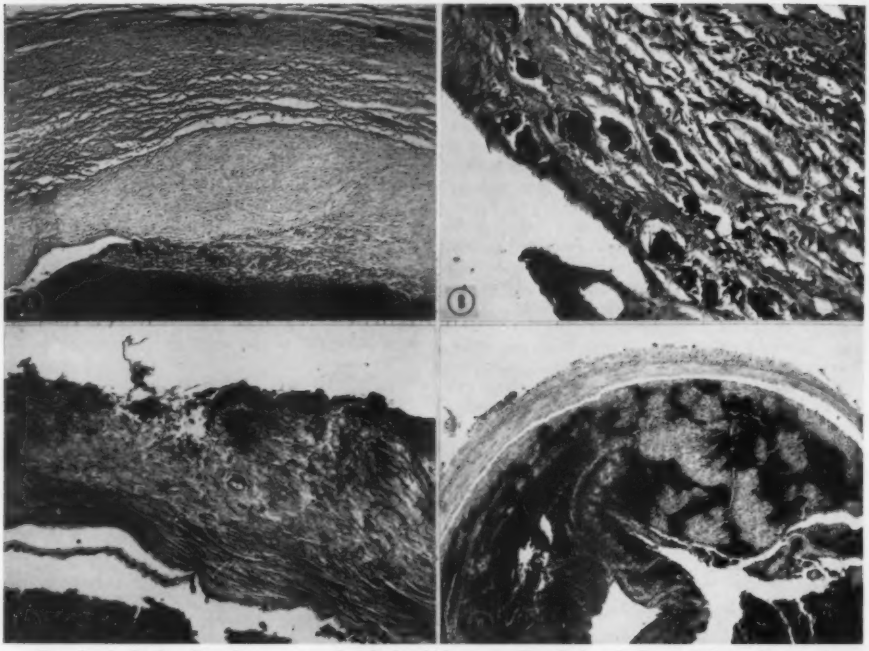

FIG. 2. *A.* Section through aneurysm of right brachial artery. The thickened, fibrotic intima, absence of elastica interna, and defective media are evident. *B.* Right brachial artery showing calcium deposition in intima and media. *C.* Left internal carotid artery with thrombus and calcium deposition in adventitia. *D.* Left internal carotid artery with organizing thrombus. Hematoxylin and eosin stain.

differential diagnosis of infantile hemiplegia. Awareness of this possibility, together with palpation of the internal carotid arteries and angiography where indicated, will undoubtedly lead to diagnosis in other cases.

From the standpoint of pathogenesis, there were histologic changes in the vessel walls which may relate etiologically to the thrombosis of the internal carotid artery. Calcium deposition was present in all coats of the brachial artery at the point of aneurysmal dilatation, together with deficiency of elastica and thinning of the media. Calcification was also present in the wall of the internal carotid artery at the level of the previously described thrombus. There was also hypoplasia of the right external iliac artery, with fragmentation of the internal elastic membrane and fibrotic thickening of the intima.

The presence of brachial and axillary artery aneurysms since birth, together with histologic alterations in the walls of these vessels as well as in the carotid and iliac arteries, makes congenital anomaly the most likely underlying condition leading to thrombosis in this case.

SUMMARY

1. A case of spontaneous internal carotid artery thrombosis in an infant is reported.

2. It is felt that the vascular abnormality in this child is on a congenital basis.

3. The causal relationship between the abnormalities in the vessel wall and the carotid thrombosis is discussed.

4. It is suggested that this possibility be considered as an etiologic factor in cases of infantile hemiplegia.

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CASE REPORT

Thyrotoxic Myopathy with Disturbance of Potassium Metabolism

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MUSCLE WEAKNESS is a common symptom and occasionally the most disabling manifestation of hyperthyroidism. That thyrotoxic myopathy may occur with little or no clinical evidence of hyperthyroidism, particularly in older patients,[1,2] is demonstrated by this case.

Muscle disorders associated with thyrotoxicosis have been classified into two groups: thyrotoxic myopathy and periodic paralysis.[1,3] A relationship between the latter and altered potassium metabolism has been demonstrated.[4] Clinically the following case resembles the thyrotoxic myopathy group more than the group with periodic muscle dysfunction. However, study of this patient demonstrated a very definite relationship between muscle dysfunction and potassium metabolism.

CASE REPORT

A 48 year old Filipino male was admitted to Fitzsimons Army Hospital on February 6, 1956 because of muscle weakness. For three weeks he had noted persistent weakness of all extremities; occasionally this had become so marked during the evenings that he had been unable to stand. He denied any history of ptosis or diplopia, but had noted some mild difficulty in swallowing and some hoarseness during the three weeks prior to admission. There was no history of previous weakness and no family history of muscle weakness or other neurologic disease. There was no history of nervousness, heat intolerance, diarrhea, or palpitations. There had been a 12 pound weight loss in the past six months.

There was moderately severe weakness of muscles of both shoulder and hip girdles, so that he could not raise his arms against more than token resistance, had difficulty stepping up on a chair, and could not do deep knee bends. Weakness of distal muscles was minimal and there was no evident weakness of bulbar muscles. There was a fine rapid tremor of the outstretched hands. No abnormalities of cranial nerves, reflexes, or sensations were noted. There was no exophthalmos, no other eye signs of hyperthyroidism, and no palpable enlargement of the thyroid. The hands were slightly moist and warm. Blood pressure was 140/82. Sleeping pulse rates varied between 70 and 80, although during the day pulse rates as high as 120 were obtained.

Routine peripheral blood studies, urinalysis, serological test for syphilis, and chest roentgenogram were normal. The basal metabolic rate was plus 28. Protein bound iodine was 13.9 micrograms per cent. Twenty-four hour thyroid uptakes of radioiodine (I^{131}) on two occasions were 81 per cent and 80 per cent. A radioiodine thyrogram revealed a normally located and normally shaped but diffusely enlarged thyroid. Microscopic examination of biopsies from the left deltoid and pectoralis major muscles revealed normal muscle.

Test doses of 1.5 and 2 mg. of prostigmine and 10 mg. Tensilon produced no improvement in muscle strength. Observation in the hospital revealed only minimal fluctuation in the degree of muscle weakness at various times of the day; moderately severe degree of weakness was present at all times.

A glucose tolerance test with serum potassium determinations was done using 100 gm. glucose orally (table 1A). Within one hour after ingestion of the glucose, the patient became profoundly weak—much more so than had been previously noted—and remained weak for the rest of the day. Three days later he was again given 100 gm. glucose by mouth and again after one hour he was profoundly weak. One hour and 20 minutes after ingestion of the glucose an electrocardiogram was normal. He was then given 2 gm. potassium chloride by mouth, and after 55 minutes the weakness had diminished greatly. However, about two hours later (after eating lunch) he again became profoundly weak and remained so throughout the day. The following day potassium chloride, ten grains given orally three times daily, was instituted. By the next day he demonstrated no weakness whatsoever, noted no subjective weakness, and stated that he felt as strong as he had at any time during the past few years. Repetition of the glucose tolerance test (table 1B) (no potassium chloride being given the morning of the test) was again associated with moderate weakness (not nearly as severe as during the previous test) that disappeared within a few hours after potassium chloride administration was resumed. He remained free of weakness for over two weeks until the potassium chloride was inadvertently discontinued when he was transferred to another ward. Two days later he again became weak, but the weakness again disappeared with the resumption of potassium chloride administration. For treatment of hyperthyroidism he was given 7.6 millicuries

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TABLE 1
GLUCOSE TOLERANCE TESTS WITH 100 GM. GLUCOSE BY MOUTH

A. Before administration of potassium chloride (March 2)

Time	*Blood Sugar*	*Urine Sugar*	*Serum K*
Fasting	109 mg. per cent	negative	5.3 mEq./l.
½ hour	290 mg. per cent	2 plus	4.1 mEq./l.
1 hour	150 mg. per cent	4 plus	4.1 mEq./l.
2 hour	101 mg. per cent	trace	4.1 mEq./l.
3 hour	85 mg. per cent	negative	3.6 mEq./l.

B. After institution of potassium chloride (March 14)

Time	*Blood Sugar*	*Urine Sugar*	*Serum K*
Fasting	126 mg. per cent	negative	5.1 mEq./l.
½ hour	232 mg. per cent	2 plus	4.9 mEq./l.
1 hour	135 mg. per cent	2 plus	4.9 mEq./l.
2 hour	135 mg. per cent	negative	4.8 mEq./l.
3 hour	97 mg. per cent	negative	4.5 mEq./l.

C. After treatment of hyperthyroidism (May 29)

Time	*Blood Sugar*	*Urine Sugar*	*Serum K*
Fasting	88 mg. per cent	negative	4.1 mEq./l
½ hour	163 mg. per cent	negative	hemolyzed
1 hour	123 mg. per cent	negative	4.1 mEq./l.
2 hour	83 mg. per cent	negative	3.8 mEq./l.
3 hour	61 mg. per cent	negative	3.9 mEq./l.

I^{131}. The potassium chloride was discontinued two months later, with no recurrence of any muscle weakness to date. Repetition of the glucose tolerance test was associated with no weakness (table 1C). Ear, nose, and throat evaluation revealed no weakness of the vocal cords, but a keratotic lesion was found (and biopsied) which probably accounted for the hoarseness.

DISCUSSION

Thyroid evaluation as a routine in cases of muscle disorder of obscure etiology, rather than any particular diagnostic acumen, in this case led to the proper diagnosis of a gratifyingly treatable disease with complete restoration to normal health.

The simple laboratory and clinical studies of carbohydrate and potassium metabolism led us to initiate potassium chloride therapy with an almost immediate "cure" of the muscle weakness while the more long-range treatment of the hyperthyroidism was underway. These studies perhaps also throw some light on the pathophysiology of this and related problems.

The fact that weakness disappeared with administration of potassium chloride indicates that the symptom resulted from potassium deficiency rather than from an excess of potassium in any of the fluid compartments. Although increasing weakness was associated with decreasing serum potassium during the first glucose tolerance test, the fact that he was weak with a serum potassium level of 5.3 mEq./l. and profoundly weak with a serum potassium level of 4.1 mEq./l. before treatment of his hyperthyroidism but demonstrated no weakness with a serum potassium level of 3.8 mEq./l. after treatment would indicate that the weakness was not directly due to a deficiency of serum or extracellular potassium. It seems likely then that the weakness was due to a deficiency or nonavailability of intracellular potassium.

The exaggeration of weakness by carbohydrate ingestion and the rather marked change in the glucose tolerance curve with treatment of the hyperthyroidism suggests that altered potassium metabolism may be related to altered carbohydrate metabolism. It is well known that potassium is intimately involved in carbohydrate metabolism. Potassium and glucose tend to move out of and into the blood together; potassium is thought to play a part in the intermediary metabolism of glucose to glycogen; the deposition of glycogen in the liver is accompanied by the deposition of potassium.[5] Potassium also is liberated from muscle with lactic acid during muscular activity as muscle glycogen is utilized.[6] Perhaps the altered carbohydrate metabolism of hyperthyroidism decreases the potassium available for the resynthesis of phosphocreatine and adenosin-triphosphate and hence results in muscle weakness.

The fact that the weakness disappeared with potassium administration would indicate that, in this case at least, the muscle weakness associated with hyperthyroidism was not primarily due to a disturbance in creatine-creatinine metabolism, as has been suggested.[1] Since creatine and potassium contents of striated muscle vary directly, increasing or decreasing together,[7] it seems more likely that the altered

creatine-creatinine metabolism is secondary to the altered potassium metabolism.

This case, which clinically demonstrated non-periodic thyrotoxic myopathy but which exhibited the same abnormalities in potassium metabolism that have been demonstrated in thyrotoxic periodic paralysis, suggests that thyrotoxic myopathy and thyrotoxic periodic paralysis may represent variations or different stages resulting from the same metabolic abnormality.

The relationships between thyrotoxic myopathy and carbohydrate and potassium metabolism should be studied extensively.

SUMMARY

1. A case is presented of thyrotoxic myopathy with minimal clinical evidence of hyperthyroidism and with complete recovery of the myopathy after successful treatment of the hyperthyroidism.

2. Associated alterations in carbohydrate and potassium metabolism were demonstrated.

3. The muscle weakness responded dramatically and repeatedly to potassium administration.

4. The pathophysiology of muscle weakness associated with hyperthyroidism is discussed.

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■ When we stand at the bedside of a patient, when we come close to our clinical work, there is before us an anatomical, a physiological and a pathological problem. A great part of our clinical knowledge of cases is really nothing more than anatomical and physiological knowledge. The word disease is too vague; it is used in three senses, each of which should be individualized. Since I am about to speak of cases of disease, it is not needful to add, were it correct to do so, the adjective morbid to the terms anatomy and physiology. I can best illustrate by diseases of the nervous system.

In each case: (1) There is alteration of structure of some organ; here is an anatomical problem. (2) There is alteration in the proper functional activity of that organ; here is a physiological problem. (3) There is a change in nutrition of tissues of that organ; here is a pathological problem. In many cases, we cannot carry out this threefold scheme. But we should attempt it in every one, in order that we may realize vividly what it is we do *not* know.

J. Hughlings Jackson in *Address on Pathology*, published in 1882.

CASE REPORT

Carotid Artery Insufficiency Corrected by Internal Carotid Thrombectomy

H. Harvey Gass, M.D. and Homer M. Smathers, M.D.

ATTENTION has recently been drawn by Denny-Brown,[1–4] Corday, Rothenberg, and Putnam,[5] and by Millikan and Siekert[6–9] to the syndrome of arterial insufficiency of the brain. Syndromes of basilar artery insufficiency and carotid artery insufficiency consisting of recurring transitory neurologic symptoms produced by temporary ischemia of the parts supplied by these arteries are being recognized with increasing frequency. Repeated transitory neurologic incidents, however, may finally be followed by an irreversible infarction, with a permanent neurological deficit or actual death. To prevent such a tragic result, Millikan and Siekert have advocated the use of anticoagulant therapy and have effectively demonstrated its value in the prevention of these repeated transient incidents.

In recent years the syndrome of internal carotid artery thrombosis has been established as a major cause of cerebral infarction and in many instances may be preceded by symptoms secondary to transient cerebral ischemia before the actual infarction takes place. Too often, however, the diagnosis of internal carotid artery thrombosis has occurred too long after the actual occlusion has occurred for anything definitive to be done to remedy the infarcted area. Even late reconstruction of the cervical carotid artery system in the neck by vascular grafts or thrombectomies would seem to be of doubtful value once the cerebral infarction is established. This has been the experience of Strully, Hurwitt, and Blankenberg,[10] and of Webster, Gurdjian, and Martin.[11] Efforts, therefore, should be directed either toward such reconstruction immediately at the time of the occlusion or toward the recognition and correction of accessible lesions prior to the moment of major occlusion. The case reported here demonstrates an incidence of the latter type corrected by excision of the thrombus prior to imminent total occlusion. This was done without the use of anticoagulant therapy, and produced relief of presenting symptoms until the time of writing nine months following surgery. Arteriographic verification of patency was demonstrated four months following surgery.

Cases showing recurring transitory neurologic deficits secondary to carotid artery insufficiency successfully treated by surgical reconstruction of the carotid artery system in the neck have previously been reported by Eastcott, Pickering, and Rob[12] and by Lin, Javid, and Doyle.[13]

CASE REPORT

A 48 year old woman had known hypertension to levels as high as 210 systolic for the previous two years. About one year before she was first seen by the writers, she began having episodes of weakness and paresthesia involving the right arm, leg, and face which recurred with increasing frequency. Characteristically the episode would begin with a heavy feeling in the right hand, which quickly ascended up the arm into the side of the face and sometimes, but not always, into the right lower extremity. Along with this there was often some difficulty in speech and expression. Sometimes there was a sense of faintness during the episode, although she never actually blacked out or lost contact with her environment. There was no associated headache. Since the onset of these symptoms she had always been cognizant of a pulsating sound or feeling in the left side of her neck. She knew, too, that that sound was diminished somewhat by putting her head backwards in hyperextension. There was no subjective intracranial bruit or tinnitus, convulsive history, or visual symptoms. At first these attacks occurred every week or two, and then gradually increased to two or three times a week. In the two or three weeks prior to our first contact with her they were occurring several times a day. During the last week of this period they occurred almost every half hour.

She admitted to being short winded at times and occasionally her ankles swelled. At times, too, there was some pain in her chest on excessive walking. However, she had never been treated for cardiac, pulmonary, or renal disease. Otherwise her general, past, and systemic histories were not contributory.

On examination her blood pressure was found to be 190/100 in either arm in the sitting position. She was a phlegmatic and obese woman. No bruit could be heard in the head. Neurologic examination was essentially negative, with the following

From the departments of neurosurgery and surgery, Mt. Carmel Mercy Hospital, Detroit, Michigan.

FIG. 1. Preoperative film. Arrow points to filling defect at origin of internal carotid artery. A slight amount of dye passes this point of obstruction.
FIG. 2. Film taken four months postoperatively showing internal carotid artery filled out at its origin. Arrow points to site of previous obstruction.

exception. When the right carotid artery was occluded manually, paresthesia and weakness in the right hand were reproduced which could be relieved promptly by stopping the occlusion. These symptoms could also be brought on by turning her head far to the right. She could squeeze a dynamometer with the right hand to 40 and with the left to 80 pounds.

She was admitted to Mt. Carmel Mercy Hospital on June 23, 1956. Chest roentgenogram was normal for lung detail, heart size, and configuration. Routine laboratory studies, including urinalysis and blood count, were within normal limits. Her blood pressure ranged between 210/110 to 194/100 on several determinations following admission to the hospital. An electrocardiogram was normal. Skull films were not remarkable. On June 26 a left carotid percutaneous angiogram was performed, and on each of several injections a sharply demarcated change in caliber of the internal carotid artery was seen just beyond the bifurcation of the common carotid artery. This change in caliber was localized and rounded suggesting a mass lesion in the internal carotid artery itself (figure 1). On the first of several of these injections, sufficient dye passed this point to fill the intracranial vessels moderately well. On subsequent injections this was not the case and very little dye passed this point of obstruction.

On July 5, under general anesthesia and with the aid of moderate hypothermia to levels of about 94.5° F. rectally, the bifurcation of the common carotid artery was exposed. With the use of small bull dog clamps occluding the external, internal, and common carotid arteries separately, an incision was made over the common carotid artery beginning above the lowest bull dog clamp, which had been applied about 2 cm. below the bifurcation, up to the internal carotid. An organized thrombus was found which measured approximately 1 cm. in length at the origin of the internal carotid artery. This specimen was easily removed by sharp and blunt dissection. The wound was then closed with a running arterial suture. When the bull dog clamps were released a patent lumen was noted and a good flow appeared to be present in the left carotid artery. The total occlusion of the arteries in the neck was maintained for approximately ten minutes while the intra-arterial work was being done. The patient's postoperative course was uneventful.

Since surgery she has been seen on several occasions and there has never been a recurrence of right-sided weakness or speech disturbance. The attacks which were occurring prior to surgery have not reappeared. There has been a minimal loss of stereognostic acuity in the right hand which is not disabling to her. This remains unchanged. Other than this item there was no neurologic deficit at the latest evaluation nine months following surgery. On November 3, 1956, four months postoperatively, a repeat left percutaneous angiogram no longer demonstrated the narrowing of the origin of the internal carotid artery. A normal sized lumen appeared to be present at this site (figure 2).

DISCUSSION

The syndrome of arterial insufficiency of the brain has been re-emphasized recently by Webster, Gurdjian, and Martin[11] as a common *modus operandi* for recurring vascular episodes involving the internal carotid artery distribu-

tion of the brain. They have demonstrated surgically on many occasions incomplete occlusions of the cervical carotid artery system at the region of the carotid bulb by plaques or stenosis in that area. In three patients they attempted the reconstruction of the bifurcation after excision of the atheromatous segment, but in each case rethrombosis occurred at the operative site. Eastcott, Pickering, and Rob[12] were the first to successfully reconstruct the internal carotid artery in the neck to prevent intermittent recurring attacks of hemiplegia. In their case recurring attacks of transient right hemiplegia and aphasia with blurred vision in the left eye appearing for five months prior to surgery in a 66 year old woman were brought to an end by the successful excision of 3 cm. of diseased segment of the carotid artery in the neck. Direct end-to-end anastomosis between the common and internal carotid arteries was done. Anticoagulants were not used in their case. For a five month follow-up period no neurologic deficit appeared. Cooley, Al-Naaman, and Carton[14] reported a successful restoration of circulation by a thromboendarterectomy in the carotid system in the neck. In their patient the presenting complaint was a swishing noise in the left ear which was corrected by this operation after demonstration by angiography of a partial occlusion of the left common carotid artery beginning just proximal to the bifurcation. A third successful case of restoration of carotid artery circulation following partial internal carotid artery occlusion has been reported by Lin, Javid, and Doyle.[13] They used a saphenous vein graft to replace the resection of a diseased segment of the vessel in a patient who had been having intractable attacks of left facial pain for several years associated with episodes of right hemiparesis.

In the present case treatment by anticoagulant therapy was considered. However, after angiographic demonstration of a discreet lesion which suggested an excisable thrombus, and particularly in view of the rather marked hypertension that this woman had, a direct attack on the demonstrated lesion was decided upon. It was hoped that during the period of surgical occlusion of the internal carotid supply to the brain greater protection to the left hemisphere would be given by the use of hypothermia. The obesity of the patient, however, prevented obtaining a temperature lower than 94.5 degrees rectally by the methods which on several previous instances had been adequate to reduce temperatures to 86 and 87° F. Nevertheless, she tolerated a total occlusion of the internal carotid artery supply to the left half of her brain for ten minutes without serious neurologic sequela. The minimal stereognostic disability with her right hand resulting from surgery is not disabling to her.

It is hoped that the successful result in this case and others reported previously will stimulate further angiographic search for discrete localized arteriographic lesions in the cervical portion of the internal carotid artery in patients manifesting carotid arterial insufficiency of the brain.

SUMMARY

A case is presented of carotid artery insufficiency of the brain produced by a thrombus at the origin of the internal carotid artery which was successfully removed surgically. Reformation of the thrombus had not occurred nine months following surgery, despite the fact that anticoagulant therapy was not used.

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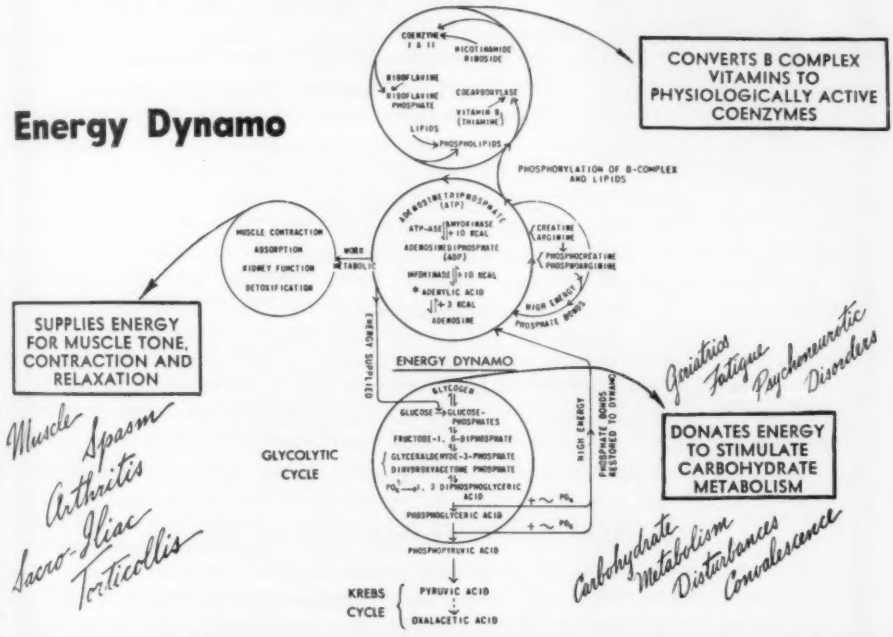

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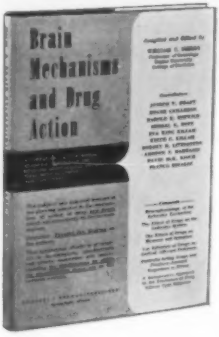

BRAIN MECHANISMS AND DRUG ACTION

A Symposium: Fourth Annual Scientific Meeting of the Houston Neurological Society, Texas Medical Center, Houston, Texas

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NEWSLETTER

AMERICAN ACADEMY OF NEUROLOGY

SEPTEMBER 1957

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International Congress Held in Brussels

Almost 3,000 neurologists and neurologic scientists from 50 nations convened in Brussels (July 21-28) for The First International Congress of Neurological Sciences (ICNS). This combined congress of neurologic disciplines, the first of its kind, comprised the Sixth International Neurological Congress, the Third International Congress of Neuropathology, the Fourth International Congress of Electroencephalography and Clinical Neurophysiology, the First International Congress of Neurological Surgery, the Fifth Reunion of the International League Against Epilepsy, and the Fifth Neuroradiological Symposium.... Held under the high patronage of His Majesty Baudouin I, King of the Belgiums, the ICNS was organized locally by a Belgian executive committee of which P. Van Gehuchten was president; L. van Bogaert, secretary-general; J. Radermecker, assistant secretary general; J. Titeca, treasurer; A. Ley, editor of transactions; and A. Dewulf, in charge of scientific exhibits.

Most Activities Centered in Palais des Beaux-Arts

The official headquarters of the ICNS was the fabulous Palais des Beaux-Arts, an underground labyrinth which houses a huge concert hall (3,000 seats); several large auditoriums; a movie theater; two king-sized exhibition halls in which there was a galaxy of neurological exhibits, scientific and technical; a bar and restaurant ("Taverne des Beaux-Arts"); and a seemingly endless number of smaller conference rooms and winding corridors.... Among the special facilities set up for the ICNS were individual secretariats for each constituent discipline of the congress, several special information bureaus, including one for the AAN, a bank, a post office, and a travel agency. Also, a selected group of the "fair hostesses" for the 1958 Brussels World's Fair assisted as guides and interpreters.

Official Registration

Registration at the secretariats of the neurological disciplines constituting the ICNS began in the Palais des Beaux-Arts, Saturday, July 20. Each member of the congress received a smart blue zipper brief case containing an identification badge;[1] a printed program; three volumes of the transactions of the scientific sessions; invitation cards to official social functions; and numerous informative

[1]Attached was a jubilee medal showing an effigy of Prof. Arthur Van Gehuchten in front and on the back the names of Babinski, Sherrington, and Horsley, whose centenaries were celebrated at the congress.

folders for sightseers and gourmets. Also included was a small attractively bound volume (royal blue) which contained resumes of the scientific sessions, the names of the officers and members of the ICNS and its constituent disciplines, and a wealth of material related to the congress.

Opening in Presence of King On Sunday afternoon (July 21), the congress was formally opened in the concert hall of the Palais des Beaux-Arts in the presence of the King of the Belgiums, the Minister of Public Health, and other officials of state. Brief addresses were made by P. Van Gehuchten, president of the congress, by G. H. Monrad-Krohn, and by the respective presidents of each constituent neurologic discipline of the ICNS. A standing ovation was extended to Secretary-General Ludo van Bogaert.... Later that evening, the Minister of Public Health Monsieur E. Leburton and Madame Leburton entertained members of the congress at an official reception in the Royal Museum of Art and History (Palais du Cinquantenaire).

Epilepsy League Initiates Scientific Program Prior to the official opening of the congress late Sunday (July 21), the International League Against Epilepsy (A. E. Walker, president) inaugurated its scientific program with symposia both in the morning (W. G. Lennox, chairman)[2] and in the afternoon (Pearce Bailey, chairman). In the latter, Henri Gastaut summarized the proceedings of the Second International Colloquium on Temporal Lobe Epilepsy held at the National Institute of Neurological Diseases and Blindness (See Feb. 1957 NEWSLETTER). The closing sessions of the League's Sunday afternoon program consisted of resumes of communications which related to either temporal lobe (C. B. Ledeboer, chairman) or petit mal (A. Asenjo, chairman) seizures. The former were summarized by Francis M. Forster, the latter by P. Passouant (Montpellier)....

General Organization Of Scientific Program The ICNS scientific program was arranged to promote the widest possible exchange of interdisciplinary thinking and cross-fertilization of personal contacts. Thus, two full days (July 22-23) were devoted to the two major topics of common interest to most of the constituent disciplines, "Extrapyramidal Pathology" and "States of Consciousness in Neurology." In addition, each constituent discipline of the ICNS conducted sessions of its own, consisting of formal reports and discussions on one or more preselected themes or topics, and free communications which had been grouped according to subject matter and were summarized by various "digest leaders." While this system of digest reporting was not always popular with authors of free communications, yet it served the practical purpose

[2]Among the contributors to the morning sessions were Macdonald Critchley (London), Grey Walter (Bristol), and Wilder Penfield. The discussors were Th. Alajouanine (Paris), A. Mosovich (Buenos Aires), F. A. Gibbs, P. Niemeyer (Rio de Janeiro), and M. Falconer (London). The presentations were summarized by A. E. Walker.

A. Kreindler (Bucharest), H. Orthner (Gottingen), J. D. French, of making available to the congress the substance of over 500 papers. Besides the major topics of common interest and the sessions of the constituent disciplines, there were four joint interdisciplinary meetings. The Epilepsy League and the EEG group held a joint symposium on the clinical and pathologic aspects of petit mal seizures (July 25) under the chairmanship of F. A. Gibbs. The neurosurgeons and neuroradiologists combined for a symposium on stereotaxic methods (July 24), which was chaired by L. Christophe (Liege) and dedicated to the memory of Sir Victor Horsley. These two groups combined again (July 25) for a joint session on supratentorial angiomas (chairman, H. Olivecrona, Stockholm). Finally, the neuropathologists and neuroradiologists met jointly (July 26) to discuss the pathology of ionizing radiations.... The highlight of the last day (July 27) of the scientific sessions was a round-table conference on "Neurology at the Crossroads," held under the auspices of the CIOMS. Among the participants were Sir Francis Walshe, I. S. Wechsler, and Macdonald Critchley.

Topics of Common Interest

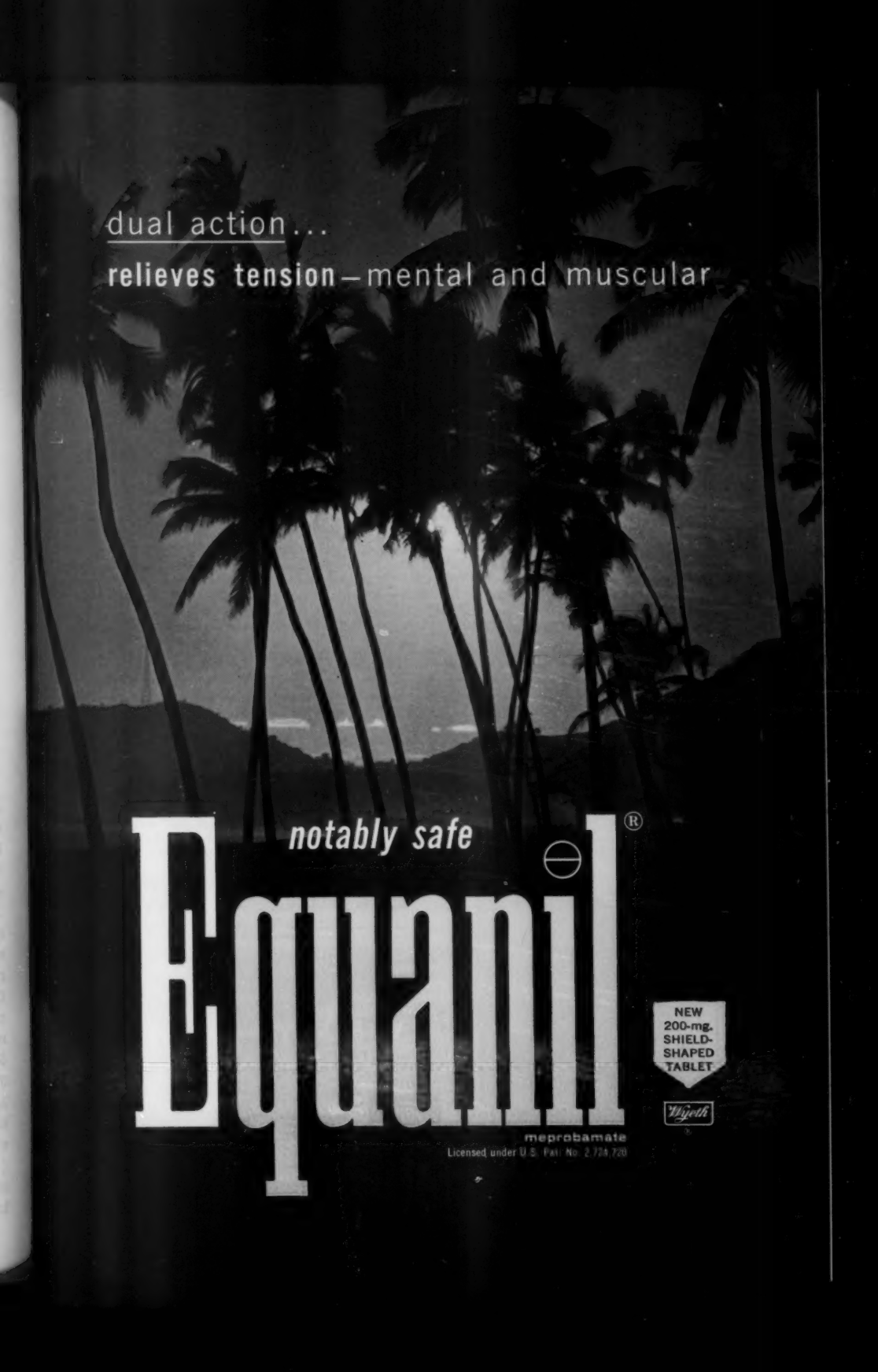
The first topic of common interdisciplinary interest on "Extrapyramidal Pathology," dedicated to the memory of Sir Charles Sherrington, was presented on July 22 under the direction of Prof. Raymond Garcin (Paris). The morning program included reports on the anatomy, physiology, and pathology of the extrapyramidal system by F. A. Mettler and J. G. Greenfield, with discussions by R. Hassler (Freiburg) and O. Trelles (Lima, Peru); a report by R. Granit (Stockholm) on systems for control of movement, with discussions by J. C. Eccles (Canberra), R. S. Schwab, and G. Schaltenbrand (Wurzburg); and reports on surgical interventions by P. C. Bucy and A. E. Walker, with discussions by H. Narabayashi (Tokyo) and G. Guiot (Paris). The morning sessions were closed with a resume by Prof. Garcin of other communications related to the central topic. The afternoon program comprised a report on the treatment of extrapyramidal diseases by D. Couto and P. Longo of Rio de Janeiro, with discussion by J. Sigwald (Paris); and a special communication by J. N. Cumings (London) on metabolic abnormalities in extrapyramidal diseases. The afternoon sessions likewise terminated with summaries and discussions by J. N. Cumings and R. Garcin of other communications related to extrapyramidal pathology.... The second topic of common interest, "States of Consciousness in Neurology," was inaugurated (July 23) by the topic director, Sir Geoffrey Jefferson (Manchester, England), with an evocation of J. Babinski whose centenary was being celebrated, which was followed by reports on centrencephalic organization by Wilder Penfield and on alterations of consciousness caused by neurological disorders by Th. Alajouanine (Paris), discussed by J. de Ajuriaguerra (Paris). Next, F. Bremer (Brussels) spoke on the physiopathologic aspects of alterations in consciousness, followed by other contributions on its physiology and anatomy by M. A. B. Brazier,

S. J. Strich (Oxford), and S. Sherlock (London). The morning sessions were concluded with a report by Percival Bailey on neurosurgical data on states of consciousness, which was discussed by Sir Francis Walshe, and by special contributions from R. Jung (Freiburg) and H. Fischgold (Paris). The afternoon sessions began with a discussion of encephalograms and vertebral angiograms of patients with altered consciousness by A. Lundervold (Oslo), followed by a presentation on the neurologic foundations of the phenomena of consciousness by V. M. Buscaino (Naples). The sessions were concluded by digests of the free communications presented by Sir Geoffrey Jefferson and Prof. F. Bremer.... Both topics of common interest were presented with simultaneous translations through an ear phone system in three languages (English, French, and German). The formal reports and discussions have been published in two volumes by "Acta Medica Belgica," 43, rue des Champs-Elysees, Brussels.

Multiple Sclerosis Provides Theme for Neurologists Multiple sclerosis was chosen as the central theme of the all day program (July 24) for the Sixth International Neurological Congress under the direction of H. Houston Merritt. After an introduction by G. H. Monrad-Krohn, the reports and discussions concerned geomedical and epidemiologic considerations by L. T. Kurland, et al., discussed by M. Halasy (Budapest) and by J. Pereyra-Kafer (Buenos Aires); immunochemical mechanisms by E. A. Kabat, discussed by B. H. Waksman and H. Tschabitscher (Austria); the neurochemistry of demyelinating diseases by G. W. F. Edgar (Amsterdam), discussed by J. N. Cumings (London), H. Pette, and H. Bauer (Hamburg); and familial incidence and role of hereditary factors by D. McAlpine (London), discussed by R. P. Mackay. The afternoon sessions were devoted to a summary of the communications on multiple sclerosis as they related to pathogenesis by Sir Russell Brain (London); to treatment by R. P. Mackay; to laboratory tests by K. Henner (Prague); and to symptomatology and geographic distribution by H. Houston Merritt.... The reports and discussions of the Sixth International Neurological Congress, as well as those of other constituent disciplines of the combined congress, also have been published by the "Acta Medica Belgica."

Other Events Information on additional aspects of the program, the gala banquet, the NEUROLOGY banquet in Antwerp, plans for future international congresses, and other events in Brussels will be made available in forthcoming issues of the NEWSLETTER.

Percival Bailey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Products and Services

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Abbott Laboratories, North Chicago, Illinois, are the producers of Harmonyl, an entirely new alkaloid of Rauwolfia canescens, identified as 11-desmethoxyreserpine. It combines the potency of reserpine with significantly fewer and milder side effects, and is recommended for transquilizing disturbed or overaggressive patients, ranging from ambulatory patients with mild anxiety tension to severely hyperactive psychotics. It is also useful for management of mild essential hypertension and as a supplement to more potent agents in severer cases.

Patients with a history of depressive episodes should be watched carefully. As with other forms of Rauwolfia, Harmonyl must be used cautiously in peptic ulcer and epilepsy and in patients about to undergo surgery or electroshock treatment. In anxiety states and other grades of mental disturbance, the dosage is 0.1 mg. to 3 mg. daily, depending upon severity of the case. In management of mild essential hypertension, 0.25 mg. may be administered three or four times daily for ten days or less, after which a maintenance dose of 0.25 mg. daily is often sufficient.

EQUANIL NOW AVAILABLE IN NEW 200 MG. TABLETS

As a means of meeting individual dosage requirements, Wyeth Laboratories, Radnor, Pennsylvania, now is marketing the tranquilizing drug, Equanil, in 200 mg. tablets as well as in the original 400 mg. size. In the new reduced-strength tablets, the drug has proved a safe and orally effective agent for the relief of anxiety, tension, insomnia, and muscle spasm. It relaxes both mind and body, does not affect autonomic functions, and has notably few side effects. For those patients in whom an individualized level of response is required, the 200 mg. tablet enables the physician to prescribe Equanil in cases where the larger tablet is not indicated.

The new scored tablets are in the shape of a shield and are marketed in "snap cap" bottles of 50. They are available on prescription only. On the market for less than two years, Equanil (meprobamate) has met with great success in relieving tenseness and anxiety brought about by the strain of everyday living. It has been endorsed by physicians throughout the country for its quick action in restoring equanimity without dulling the senses.

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WILLIAM HARVEY TERCENTENARY

The Wellcome Historical Medical Museum and Library, located at 183 Euston Road, London, was among the many institutions arranging an exhibition in connection with the 300th anniversary of William Harvey, the discoverer of the circulation of the blood, who died on June 3, 1657.

Sir Russell Brain, president of the International Society of Internal Medicine, which will be holding its Fifth International Congress next April in Philadelphia, opened the Wellcome exhibition at 6:00 p.m. on Monday, June 3. The exhibition was designed to illustrate Harvey's life, as well as to show the development of the ideas which led to his great discovery. The Wellcome Library's unrivalled collection of the various editions and translations of Harvey's books, from the first edition of the short treatise in Latin in which in 1628 he announced his epoch-making discovery to the world, up to the latest English translation to be published on his anniversary by the Royal College of Physicians, England, enable the library to stress aspects of Harvey's life which cannot be done elsewhere. Personal original documents on view include the original probate copy of Harvey's will, granted to his brother Eliab in 1659, and a letter passing for payment a bill for £15 for drugs supplied to the household of Charles I in 1637. The letter is signed "Will Harvey," in his capacity as physician to the unfortunate king.

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